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THE TECHNIQUE OF NAILING OF FRACTURES OF THE NECK OF THE FEMUR

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I. INTRODUCTION

PATIENTS with fractures of the neck of the femur very often are in poor general condition. Not infrequently the treatment is made difficult by complications, such as great age, senile debility, hardening of the arteries, lesions of the cardiovascular system, emphysema, bronchitis, kidney lesions, and so forth.

In high degree this applies to patients admitted to the public hospitals, a category in which the Ullevål Third Surgical Service belongs. While the material in the private clinics as a rule is selected, the public hospitals have to take care of numerous patients in exceedingly poor condition with fractures of the neck of the femur. This material has always represented a *crux medicorum*.

The poor general condition of the patients demands, before all, gentle treatment, medically as well as from a hospital-technical point of view. Major operative intervention and other exacting methods cannot be adopted as routine treatment for these patients.

We are aware from previous experience that even the so-called conservative treatment of Whitman-Löfberg[1] may represent a great strain upon the patient's resources. This method, furthermore, has not been used previously in a very great percentage of the material of the Third Surgical Service.

Also, from a hospital-technical point of view, this group of patients represents a problem. The slow and poor healing of the fracture has necessitated a lengthy stay in the hospital, in some cases for more than one-half to three-quarters of a year. The poor general condition and the fracture itself have made the nursing very difficult and troublesome to the patient as well as to the hospital staff.

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Reduction of the fracture should be carried out as quickly as possible after the accident, for many reasons. When admitted into the hospital, however, these patients often are greatly exhausted due to the trauma itself. The injury and the fracture cause a considerable reaction in many of these patients who are delicate beforehand (such reactions, for example, as circulatory deficiency, rise in temperature, pulmonary complications) with the result that the situation may be difficult to judge shortly after the accident.

It has been the practice, therefore, in several hospitals to leave the patient with the fracture unreduced for eight to ten days after the accident, thereby allowing this primary reaction to subside.

It is disadvantageous, however, to allow the patients to lie with the fracture unreduced. Deformity causes pain; the nursing becomes difficult. The ends of the fracture may exert pressure on the large vessels, cause circulatory deficiency and thrombosis of the vessels in the leg.

Reduction on a traction table also frequently constitutes a considerable strain on these patients. It calls for general or spinal anesthesia. The change of position alone, the rough manipulation, and the handling of the patient easily cause circulatory embarrassment. Some years ago two cases of sudden death occurred on the Third Surgical Service during reduction of fractures of the neck of the femur done on a traction table. One of these was verified as being due to pulmonary embolism.

These experiences teach us that the reduction of fractures of the neck of the femur should be performed as quickly as possible after the accident and as gently as possible, preferably without the aid of general anesthesia and without use of a traction table.

This is obtained by using Kirschner or Johansson wire traction for the reduction of the fracture carried out immediately, or as quickly as possible, after the accident. Schilling, the previous chief of the Third Surgical Service, for many years had used wire traction and Steinmann pin traction for the reduction of fractures of the neck of the femur, in part as preliminary treatment prior to a subsequent plaster treatment, in part as independent treatment, particularly of lateral fractures.

Wire traction may be applied under local anesthesia without causing any strain on the patient. Experience has proved that by this method an excellent reduction may be obtained in a simple manner.

In order to ensure an effective internal rotation of the lower fragment, I have constructed a rotative splint which makes the reduction by traction easier and more effective.

When the fracture has been reduced by wire traction, one may keep, without need for haste, the patient under observation, and one may postpone further treatment until the first reaction after the trauma has subsided. One has the opportunity then of judging the general condition of the patient correctly. Reduction and fixation of the fracture by wire traction also facilitates the nursing of the patient.

Fixation of the Fracture.—Fractures of the neck of the femur need fixation of very long duration in order to ensure firm union; lateral fractures from three to four months; medial fractures, one-half to one year.

Prolonged immobilization by plaster (as by the Whitman-Löfberg method) entails danger of pulmonary complications, circulatory deficiency, intestinal complications, bedsores, and so forth. Prolonged immobilization by traction is tolerated better by the patients, although recumbency for one-half to one whole year always means a great strain on the patient. Lengthy immobilization of patient and extremity is unfavorable, also, for the functional result, causing as it does muscular atrophy and contracture of joints.

At an early period, nailing of fractures of the neck of the femur was used to a considerable extent by Scandinavian surgeons. Nicolaysen (Oslo)[2] in 1879 demonstrated some cases which had been nailed percutaneously.

Schilling[3] in 1915 to 1916 constructed a square nail which he used for percutaneous nailing after reduction and plaster.

Smith-Petersen[4] (Norwegian born) introduced his open reduction at Ullevål in 1929. During the years 1931 to 1934 five, eleven, sixteen, and sixteen nailings respectively were performed on the Ullevål Third Surgical Service. Experience then taught us that the nail had to be made of rustless steel, as otherwise it might cause aseptic necrosis due to electrolysis.

Smith-Petersen's construction of the three-flanged nail for internal fixation has made it possible to effect a reliable fixation of the fracture without immobilizing the entire patient correspondingly.

The available end results also definitely indicate that this method offers considerably better chances of bony union than any other method.

Efforts in recent years have been concentrated on simplifying Smith-Petersen's original open operation.

As early as 1931 Schilling used a guide wire to aid in the insertion of the nail, along the wire, as well as a nail model with a cannulated head for accommodating the guide wire. At about the same time, Schilling, and independently of him another Norwegian, Backer-Grøndahl,[5] fixed the fracture with the aid of three wires which were inserted percutaneously and by this method, the so-called "wire nailing," obtained some good results.

Smith-Petersen himself has abandoned the traction table and now performs manual reduction of the fracture on the operating table immediately prior to the operation. The nail is inserted through a small incision under roentgenographic control.

Johansson's[6] and Jerusalem's constructions of the cannulated nail (1932) has meant a simplification of, and a certitude of correct direction of, the nail, and gives an exact and easy determination of the proper length of the nail.

In order to make the nailing as gentle as possible, we have in recent years at the Ullevål Third Surgical Service performed the nailing with the patient in bed, so as to avoid the use of the traction table.

THE AUTHOR'S METHOD

Immediately after admission to the hospital, wire traction is applied with the leg on a specially constructed rotative splint. As a rule an ideal reduction is obtained in the course of a few days by this method. The patient is observed and the indications for, as well as the most favorable time for, operation may be determined. When the general condition of the patient allows it, he is moved in his bed to the operating room and the nailing is performed with the patient lying in bed, traction being maintained.

The nailing's being performed with the leg on a splint, flexed in the hip joint, has made it necessary to construct a special alignment or sighting apparatus to facilitate the centering of the nail in two planes.

The advantages of this procedure are the following: It gives a speedy and good reduction of the fracture. The time for carrying out the operamay be chosen regardless of the reduction, when the condition of the patient permits. The operation need not be hurried into. One reduction only is necessary. The leg remains in the same position and on the same splint from the time of the reduction, immediately after admission, until after the nailing. One avoids the traction table, rough manipulation of the patient, and lengthy general or spinal anesthesia. The operation is relatively easy to perform.

The classification of fractures of the femoral neck has been simplified in accordance with the outline of *Anschütz:*

1. The *medial*—fractures in the narrow, medial end of the femoral neck.

2. The *lateral*—fractures in the transition between the femoral neck and the trochanteric region. In addition to these are:

3. The *pertrochanteric* or *intertrochanteric* fractures respectively in the actual trochanteric region.

The medial fractures are distinctly separated from the other two groups, and should not be confused with these.

Because of the poor condition of nutrition of the central fragment and the great tendency to pseudarthrosis, the treatment of medial fractures presents great difficulties. The prognosis is considerably better for the lateral and pertrochanteric fractures. These latter two groups have been considered together.

II. INDICATIONS

A survey of the treatment of all fractures of the neck of the femur admitted to the Third Surgical Service during a given period, a total of 157 cases, illustrates the indications for the methods of treatment used (Table I).

TABLE I

157 CASES OF FRACTURES OF NECK OF FEMUR (1935-1937)

		TOTAL	NO TREATMENT	WIRE TRACTION ONLY	TRACTION + WIRE NAILING	TRACTION + NAILING
Lateral and pertrochanteric fractures	1935	5	0	0	2	3
	1936	13	0	2	3	8
	1937	20	2	11	1	6
	Total	38	2	13	6	17 (45%)
					23 (60%)	
Medial fractures	1935	24	0	0	4	20
	1936	51	0	4	1	46
	1937	44	2	7	1	34
	Total	119	2	11	6	100 (84%)
					106 (89%)	
Medial, lateral, and pertrochanteric fractures	Total	157	4	24	12	117
					129	

Indications for Application of Wire Traction on Special Splint.—As far as possible all fractures of the femoral neck are treated with wire traction immediately after admission to the hospital. This applies to the medial as well as to the lateral and trochanteric fractures. This has been performed in a total of 153 of 157 cases (97 per cent).

Three patients only were regarded as being too ill for this treatment, and all three of them died shortly afterward. In one case, an impacted medial fracture in valgus position, the treatment was regarded as superfluous.

The primary object in the application of wire traction on the adjustable rotation splint is reduction and fixation of the fracture, but in some instances only immobilization is desired; i.e., impacted fractures in good position. In the majority of medial, and in some of the lateral, fractures this constitutes the treatment preliminary to the subsequent operative fixation.

The treatment with wire traction makes possible observation and evaluation of the general condition of the patient, and thereby gives the correct indications for operative treatment.

During this observation, some cases of medial fractures are found to be too ill for operation (a total of 11 of 119 medial fractures in this material). The wire traction furnishes an excellent palliative treatment for these very ill patients (10 of 11 died in the hospital and 1 was insane), as it relieves the pain and, the chief advantage, facilitates the nursing.

In some lateral and in the majority of the trochanteric fractures, traction on the described splint represents the chief treatment of the fracture.

Indication for Operative Treatment is not the same for the medial as for the lateral fractures. The medial fractures should be nailed to as

great an extent as possible. As far as firm union is concerned, nailing appears to yield better results than all other methods. It reduces the time of treatment and makes possible the mobilization of the patient, both within a reasonable length of time. Nailing may be indicated also for the patients who were ill, more or less bedridden, before the fracture occurred as it serves to facilitate and improve the nursing of these patients.

For these various reasons, nailing is the method of choice, practically speaking, in all cases of medial fractures of the neck of the femur. As a rule, impacted fractures also should be nailed. Furthermore, we have not made any exception for fractures with a fairly horizontal fracture surface (Pauwels[7]).

Nailing is unnecessary only in those cases where the fracture is so firmly impacted or so incomplete that plaster bandage or other immobilizing bandage is superfluous. In my material only one such case is found in 119.

The chief object of the development of my method has been to make it so gentle that it may be used in as many of these cases as possible. With this method, preliminary treatment of the patient with wire traction and nailing in bed under local anesthesia, the immediate postoperative reaction has been slight; in no single case has it been threatening. This justifies extensive use of the nailing procedure.

As mentioned before, however, these patients are frequently in poor general condition and are able to stand very little strain. The indication for nailing, therefore, should not be determined until after observation and preliminary treatment for some time. Nailing immediately after the accident is contraindicated as it entails greater risk and because it is quite superfluous.

One should wait, as a rule, for at least one week in order that the patient may recover from the trauma. If one is in doubt, nothing is forfeited by waiting for a longer period.

The fracture remains unchanged in traction until after the nailing, and during this time the patient is accessible to preliminary treatment.

By varying the length of this period of observation and preliminary treatment according to the individual patient, one is able to get as many of the patients as possible in such shape that they can well tolerate the intervention. In this way the indication for nailing is increased to an optimum.

The duration of this period of observation and preliminary treatment varies greatly, from eight days to several months.

The age of the patients with nailed medial fractures appears in Table II. In this material, nailing has been performed in 100 patients with medial fractures of the femoral neck, of which 78 patients were more

than 60 years of age; 51 patients, more than 70 years of age; and 14 patients, more than 80 years of age.

TABLE II

AGE OF PATIENTS WITH NAILED MEDIAL FRACTURES

AGE	NUMBER
Under 40 years	3
From 40 to 49 years	5
From 50 to 59 years	14
From 60 to 69 years	27
From 70 to 79 years	37
From 80 to 89 years	14
	100

The preoperative complications can be seen from the table: debility, hardening of the arteries, heart disease, apoplexy, cerebral syphilis, insanity, diabetes, asthma, and so forth. None of these lesions are regarded as definite contraindications.

In spite of preliminary treatment, some of the patients are too ill to stand any operative intervention whatever. In this material this was the case with a total of 11 patients, and these were treated with traction only. *Ten of these 11 patients died in the hospital.* This shows that the indication for nailing has been very radical. It indicates also that the method of observation used has been effective, having spared these 10 desolate patients a superfluous nailing.

The circumstances seem to demonstrate that some patients (in this material approximately 10 per cent) are so ill and exhausted after the fracture that they die regardless of the treatment to which they are subjected.

In some of the cases of ill patients who are observed during treatment with traction, the decision may be very difficult and may depend greatly on a personal estimate and personal experience.

A total of 119 medial fractures have been admitted, of which 117 have been treated with traction on admission (98 per cent). Of these 117 patients, 100 have been nailed and 6 "wire nailed," while 11 were too ill for nailing.

The material proves that this procedure supplied us with a treatment which makes possible the use of nailing as method of choice in 84 to 89 per cent of all cases of medial fractures admitted; that is to say, practically all the cases which are suitable for any active treatment at all.

In 6 cases of medial fractures so-called "wire nailing" has been performed. This method is relatively little used now, because it does not offer essential advantages in preference to ordinary nailing of medial fractures. It is not so certain in its effect; the wire easily slips out, and it calls for a more lengthy recumbency. It may be used in some

very ill patients in cases of impacted fractures in good position. This method may have a somewhat wider use in lateral and trochanteric fractures.

The lateral fractures or trochanteric fractures, respectively, in themselves have a relatively greater tendency to bony union within a reasonable time, and indication for operation, therefore, is more restricted than for the medial fractures.

The advantage of the nailing of these fractures is a shortening of the course and a better functional result, less atrophy and less contracture than occur in the use of its competitor, the traction treatment or plaster treatment.

Some of the patients with lateral fractures, i.e., those in fairly good general condition, have been nailed, and in addition some patients in whom the traction treatment has not given union in good position. The pertrochanteric or intertrochanteric fractures, respectively, are not generally suitable for nailing due to splintering of the trochanteric region so that the nail does not get a good grip.

A total of 17 of 38 of these fractures have been nailed, about 45 per cent.

III. TECHNIQUE

The Reduction.—A very accurate reduction of the fracture, controlled in two planes, is a necessary condition for the nailing.

The wire traction is usually applied through the tibial tuberosity (the lower end of the femur may also be used) under local anesthesia. Extension is obtained with twelve to twenty-four pounds (or more) of traction, varying in accordance with the size of the thigh muscles. In this way shortening is combated fairly easily; traction also increases abduction of the femur in relation to the pelvis.

It is not necessary to attain marked abduction; 10 to 15 degrees is sufficient. Too strong abduction may be unfavorable to reduction.

Flexion in hip and knee joints furnishes the most effective relaxation of the muscles. Furthermore, a flexed hip joint gives relaxation of the anterior part of the capsule with the strong iliofemoral ligament. The disadvantage inherent in the application of an ordinary straight Braun's splint is insufficient internal rotation of the lower fragment. I have succeeded in obtaining an effective internal rotation by the construction of an adjustable, rotative splint which permits maximum internal rotation of the femur (see Figs. 1, 2, and 3). The distal half of this splint, "the leg part," may be rotated in relation to the proximal half, "the femur part." The distal part of the splint with the lower leg is used as a "handle" with which the femur is rotated inward by swinging the foot and lower leg outward. The splint permits adjustment of the leg part and femur part to different lengths and with varying degrees of flexion in hip and knee joints.

Roentgenographic control of the position is carried out easily by exposure in two planes (see Figs. 4, 5, and 6). If the x-ray control film shows that the position is not ideal, it may be gradually corrected. The traction may be increased or reduced by changing the weight; the rotation may be increased or reduced by rotating the leg part of the splint. By means of this slow reduction, traction and internal rotation are obtained simultaneously and gradually, which appears to be the ideal procedure. This method of reduction does not necessitate general or spinal anesthesia.

The method has furnished excellent reduction in 98 per cent of all the cases of medial fractures in this material. In the first cases, however, this rotative splint was not used (Table III). In only two cases has it been necessary to perform manual reduction in spinal anesthesia. In these two cases the fracture surface has been irregular and with a

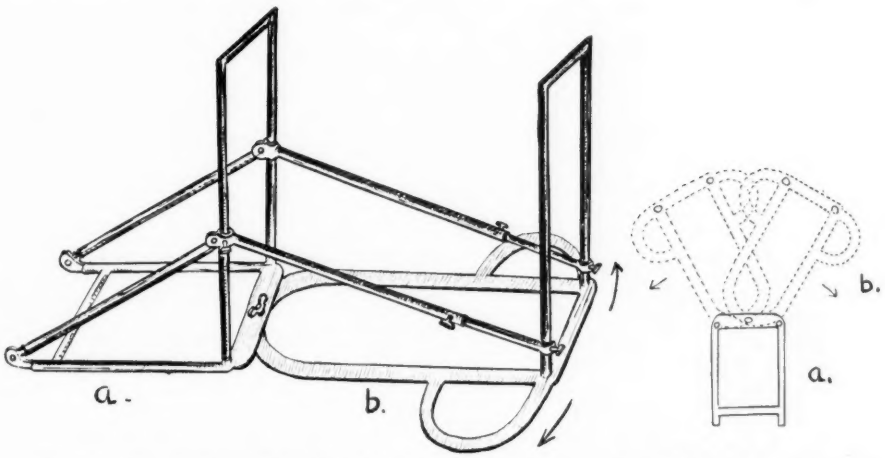

Fig. 1.—Rotatable splint (Semb) for wire traction and rotation of the femur; *a*, the "femur part," adjustable to different lengths and different degrees of flexion in hip and knee joint; *b*, the "leg part," adjustable to different angles in the knee joint and rotative, the femur is rotated inwards by swinging the "leg part" outwards.

distinctly oblique course (refer to "Pauwels III"). A protruding part of the lower fragment has hitched on to the fracture surface of the upper fragment and has rotated this backward during the internal rotation.

Complete relaxation in spinal anesthesia and manual reduction have given satisfactory results in these cases. When reducing these fractures, lateral traction is first applied according to Contremoulin and Robineau,[6] and then reduction according to Smith-Petersen's method with the hip flexed at 90 degrees and with simultaneous internal rotation.

The lateral fractures have presented no particular difficulties with regard to reduction.

In pertrochanteric fractures, splintering may make a complete reduction difficult. In spite of this, however, these fractures may heal.

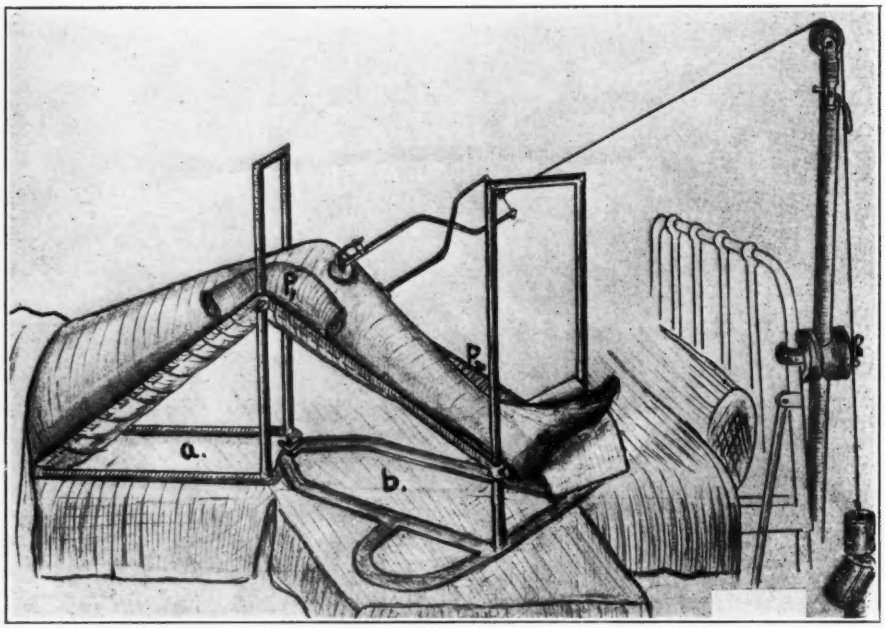

Fig. 2.

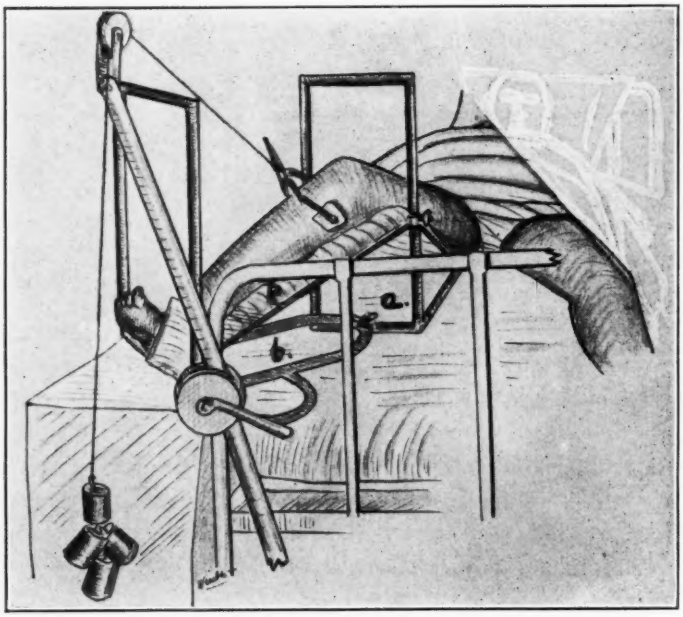

Fig. 3.

Figs. 2 and 3.—Wire traction on a rotative Semb splint. Application of the traction through the tibial tuberosity, slight abduction, flexion in hip and knee joint. The "leg part," *b*, is rotated outwards whereby the femur is rotated inwards P_1, P_2 are pads.

The method of reduction used, with wire traction on the internal rotation splint, has furnished remarkably good results, satisfying even the most exacting requirements. This is particularly the case with the medial fractures.

It is probable that it is simply this slow traction, during which the extension and the internal rotation act fairly simultaneously and in a gentle manner, which is the most favorable treatment of these fractures. The limited degree of abduction may also be of importance in obtaining good results.

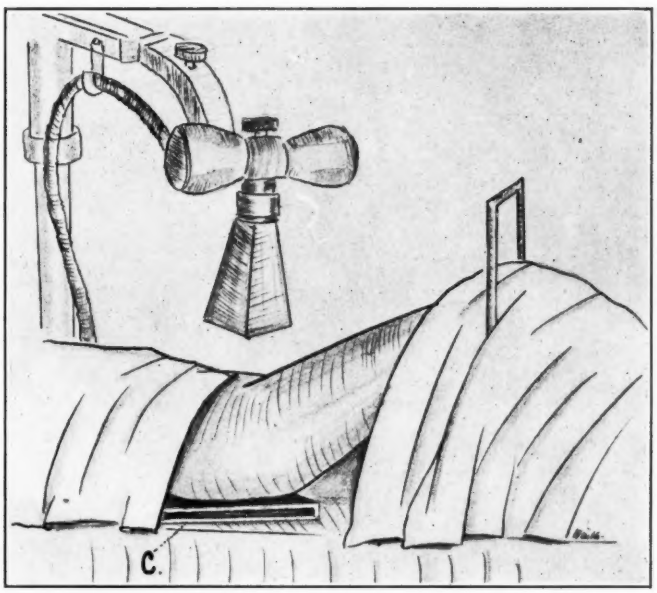

Fig. 4.—X-ray in the anteroposterior plane. A wooden cassette-holder (*c*) is placed under the splint and patient for changing films without lifting the patient.

THE OPERATION

As mentioned, the actual nailing is performed with the patient lying in bed and the leg in unchanged position on the splint with constant traction maintained (Fig. 7). A modified Smith-Petersen-Johansson technique is used.

In order to be able to take roentgenograms easily during the operation, a wooden cassette-holder is placed under the splint and patient, enabling change of x-ray films for exposures in the anteroposterior plane without moving or lifting the patient (Fig. 4). For lateral exposures, the x-ray machine is placed in the groin; the unaffected leg is lifted (Figs. 5 and 6). A curved cassette is not necessary. It is an advantage to be able to use two x-ray units at the same time.

Anesthesia.—Infiltration anesthesia corresponding to the incision below the greater trochanter as well as anesthesia of the fracture line and the hip joint are employed.

As anesthetic agent, a mixture of ½ per cent of novocain (1:200) and one-half per mille of pantocain (1:2,000) in equal parts is used. This mixture furnishes anesthesia with a duration of approximately three hours.

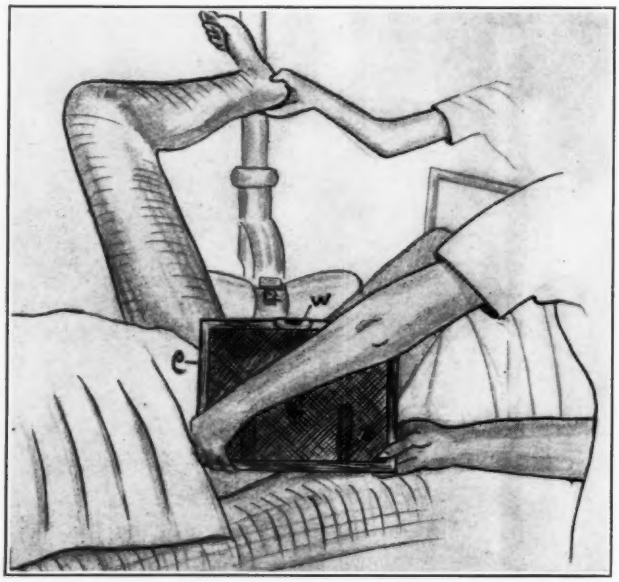

Fig. 5.

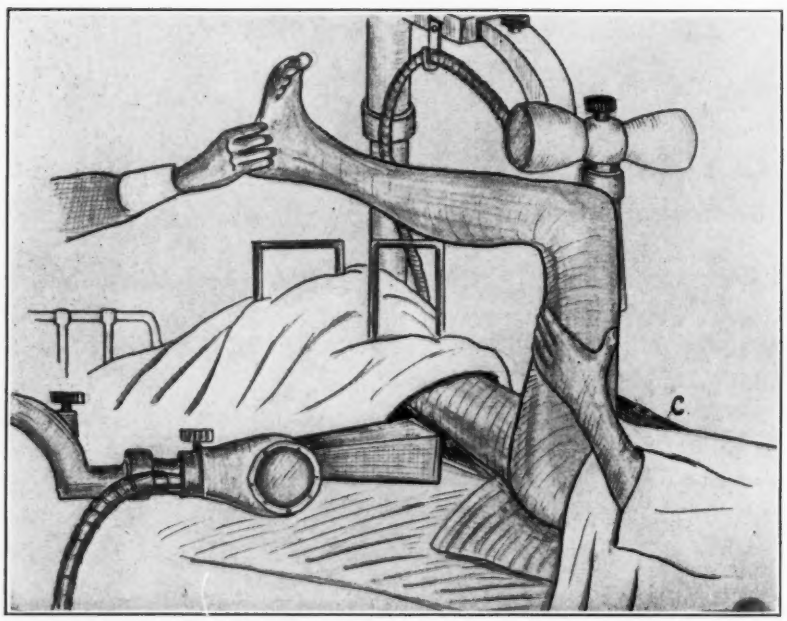

Fig. 6.

Figs. 5 and 6.—X-ray in the lateral plane. X-ray machine in the groin. A wooden cassette-holder (*c*) outside the trochanter region parallel to the femoral neck. The cassette is furnished with a water level (*w*) (see Fig. 7). Fig. 6 demonstrates the use of two x-ray units.

During the introduction of the nail, the patient is given a little gas, ether, or evipan soluble for a few minutes.

Alignment of the Wire.—An accurate centering of the nail in two planes is a necessary condition for a good result in nailing. Before the actual operation commences, metal markers are placed for alignment

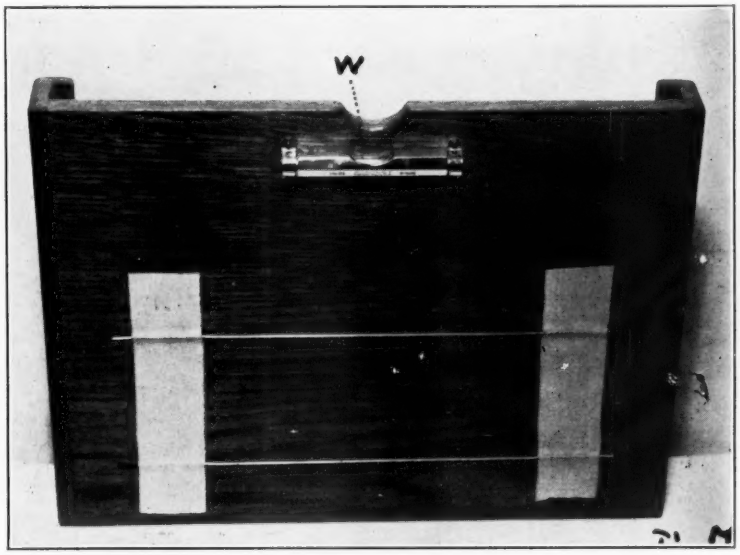

Fig. 7.—The cassette-holder for x-ray in the lateral plane; a water level and two wires parallel with this.

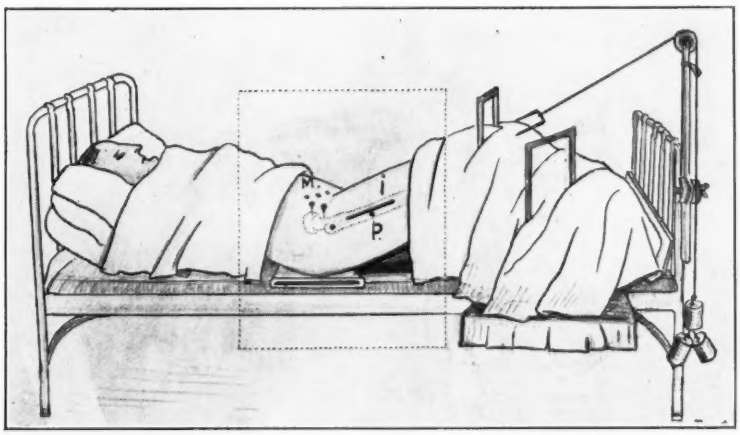

Fig. 8.—The operation is performed under local anesthesia with the patient lying in bed, the wire traction on the splint being maintained. *M*, metal markers on the skin in the groin for alignment in the anteroposterior plane; *P*, pin as a marker for the point of insertion of the nail.

and orientation. Three or four metal clips are fixed to the skin fold in the groin as alignment marks in the anteroposterior plane. Sighting at these marks is very easy with any kind of sighting apparatus. In the case of my model, this is accomplished by a curved arm which points directly at the place or mark at which one wishes to aim.

In order to get a landmark for the insertion point of the wire into the femur, a pin is driven into the femur just distal to the greater trochanter laterally. The actual point of insertion is located in accordance with the center of the thickness of the femur about 2 cm. below the trochanter.

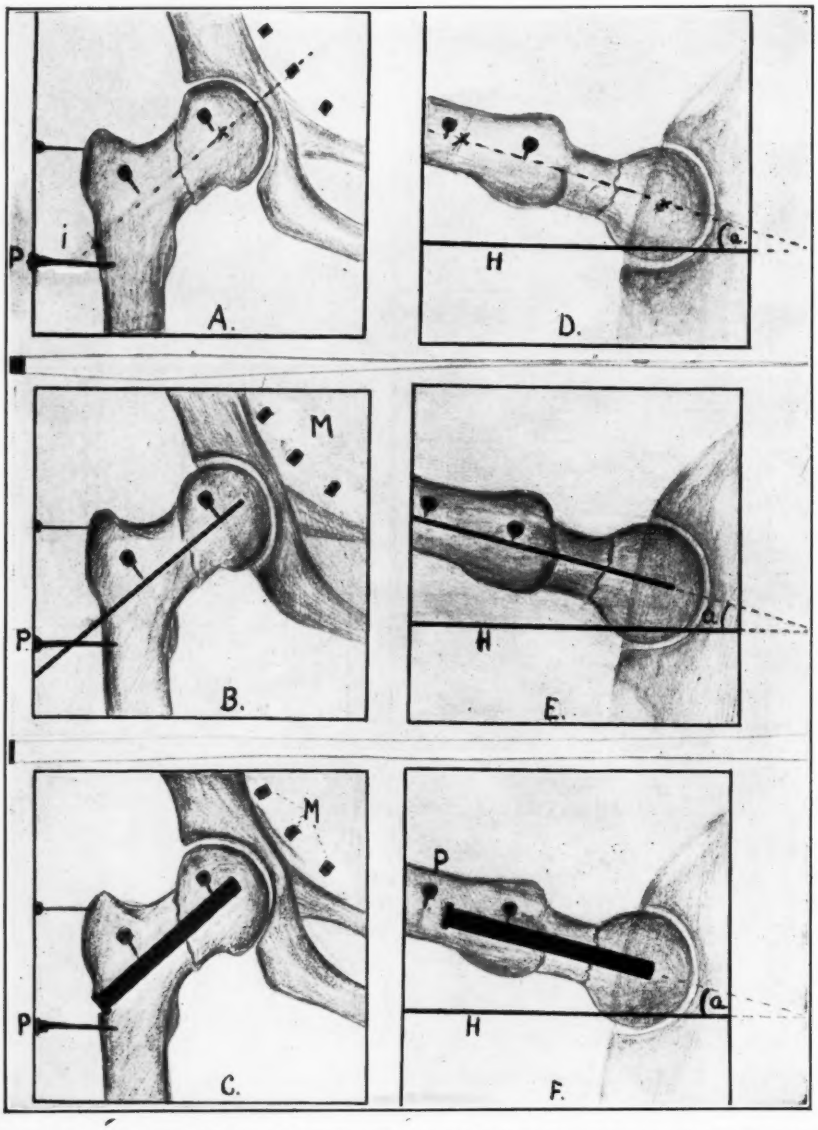

Fig. 9.—Insertion of wire and nail. X-ray control in two planes; *A*, *B*, *C*, antero-posterior plane; *M*, markers in the groin; *P*, pin for the insertion point; *D*, *E*, *F*; lateral plane; *H*, horizontal line *a*, angle between the femoral neck and the horizontal line.

The sighting in the lateral plane is more difficult. Because of the flexed position on the splint, the femoral neck forms an angle of 15 to 30 degrees with the horizontal plane. It is difficult to estimate this

angle when introducing the wire. I have endeavored, therefore, to measure this angle exactly on the roentgenogram in each separate case and to register this angle on a sighting apparatus.

The horizontal forms for this purpose the firm, unchangeable basis.

It is possible to reproduce the horizontal line on the roentgenogram by supplying the cassette-holder with a water level and one or two wires parallel with this (Fig. 7). The central axis of the neck of the femur is marked on the x-ray film, from the point of insertion decided on for the wire to the center of the femoral head.

As no previously known sighting apparatus can be adjusted to definite angles to the horizontal plane, I have constructed my own sighting apparatus for this purpose (Fig. 10). On the sighting apparatus also the horizontal line is marked by a water level.

The sighting apparatus is supplied with a scale for adjustment to a given angle to the horizontal plane; i.e., the water level. When during the drilling the level is held horizontally, the wire consequently must be inserted into the femur at the desired angle to the horizontal plane.

With the aid of this sighting apparatus of the author's, therefore, one is able to adjust the wire in two planes in accordance with the anteroposterior and lateral roentgenograms.

By accurate marking and by photographing in correct planes, vertically and horizontally, and by accurate aim, the wire in most cases enters correctly at the first attempt. An incorrect direction may be rectified by another wire.

The constructed sighting apparatus is affixed to an electric drill in order to avoid the inaccuracy of manual drilling.

A drill is used which is supplied with a point constructed by Haugland and which "shoots" the wire out of the handle. This prevents displacement of the sighting apparatus during the drilling. The actual sighting apparatus, of course, may be affixed to any kind of drill.

The sighting apparatus has been constructed so as to be as simple as possible. For this reason it has been prepared for free adjustment without being fixed to the bed.*

From our material one can see that, in the first cases, i.e., where we did not as yet have the sighting apparatus, we frequently had difficulty, especially in the lateral plane, in centering the wire or the nail accurately. Since we began to use the sighting apparatus and skin clips and pins as markers, as described, this difficulty has been overcome. As a rule the guide wire enters the center of the femoral head on the first attempt.

*This apparatus is manufactured by Norsk Medicinsk Varehus, Oslo, Norway, where the rotative rotation splint also may be obtained.

The incision is made immediately before the insertion of the wire. It should be made about 1 to 2 cm. anteriorly to the middle of the trochanter and femur because of the tendency of the soft parts to sag (Figs. 8 and 11). The wound edges should be carefully covered by compresses which are fixed with sutures. Metal clips interfere with the roentgenograms.

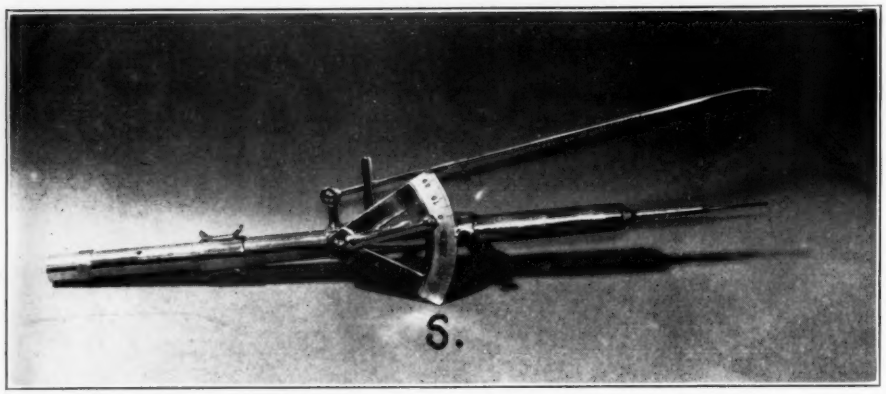

Fig. 10.—The sighting apparatus (Semb). A curved arm (*a*) for sighting at the markers in the groin. A scale (*s*) with water level for adjustment to a given angle to the horizontal plane.

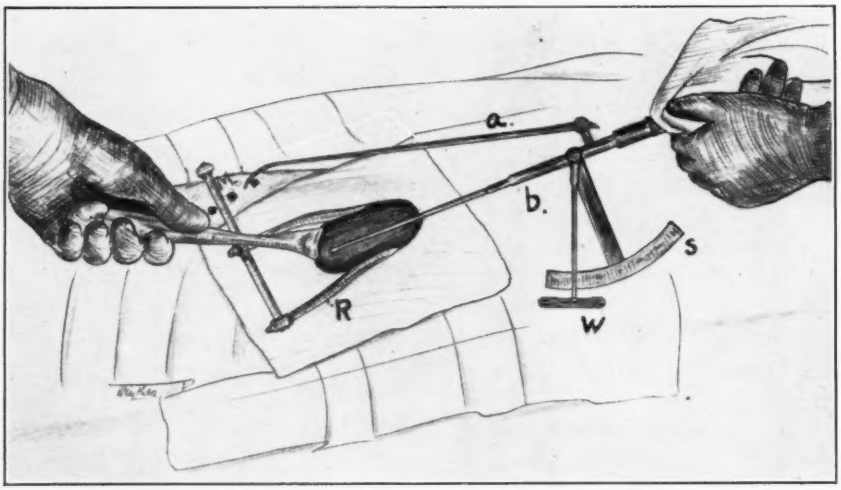

Fig. 11.—The use of the sighting apparatus (a somewhat older model). *a*, the curved arm pointing at the marker in the groin; *b*, the drill with the wire at a given angle with the horizontal plane; *w*, a water level giving the horizontal line; *S*, scale for adjustment to the given angle; *R*, self-retaining retractor in the incision; *M*, markers in the groin.

The point of insertion for the wire is found with the guidance of the pin (Fig. 9, *P*) which was driven in as a marker. If the femur is thick and firm, a groove should be chiseled out for the nail. If the bone is brittle, this is not necessary.

The length of the nail to be used is determined in relation to the wire. All wires present on the operating table are of exactly the same

length. The length of the drilled-in part of the wire is easily determined by subtracting the length of that part which remains outside the bone from the standard length. It is important to calculate the length of the nail accurately.

One should make allowances for 3 to 5 mm. shortening of the neck of the femur during impaction and driving-in of the nail. The nail should not enter further than to about ½ cm. from the surface of the head of the femur.

Prior to the final driving-in of the nail, the length and position are controlled by x-ray. A somewhat shorter nail may be inserted a little further than usual; a nail which is a little too long, less than usual.

In my opinion the nail should be fixed against the femur to prevent subsequent extrusion. This may be done by driving it so far in that

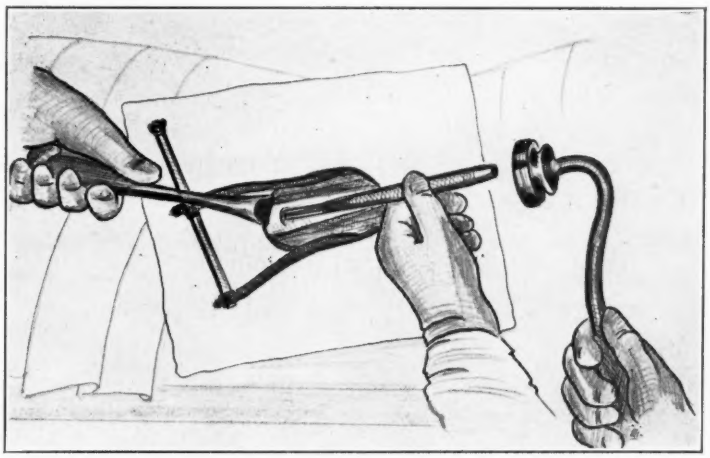

Fig. 12.—Insertion of the cannulated nail.

the lower edge of the head of the nail is supported against the external lamina of the femur (Fig. 9, *C*). The nail will hitch on and will not slip out. After some time has elapsed, it becomes entirely or partly covered by callus from the femur (Fig. 13, Case 24). This also prevents the nail head from irritating the soft parts and forming a painful bursa, which is demonstrable in cases where the head of the nail penetrates into the soft parts.

It has been held that, following a subsequent absorption of the femoral neck, the nail may become too long. The risk of this is so small that it cannot by any means outweigh the safeguard obtained by this technique against outward slipping.

After impaction of the fracture, the incision is sutured without drainage. The traction is removed immediately. The leg is placed on an ordinary Braun's splint.

This operative technique is, above all, simple. In my material it has been used not by a specialist, but by all the assistants on the service—in all, ten different operators. Most of these had never undertaken a spiking previously.

Since the patient lies relatively comfortably in his bed and since the surgery is done under local anesthesia, one can work at leisure and use as much time as is necessary for an exact carrying out of the procedure. With this technique it is possible to satisfy the two most important requirements for this successful operation: (1) an absolutely exact reduction of the fracture before the nailing and (2) an absolutely exact centering of the nail.

Postoperative Treatment.—The skin sutures are removed on the seventh day. At the same time, the splint is removed and the leg is left free in bed. If the wound has healed, energetic exercise therapy is instituted with active movements in hip, knee, and foot joints.

Generally the patient is kept in bed for eight weeks after the operation. This time has been chosen at Nystrøm's[8] suggestion.

It must be assumed that premature weight-bearing may reduce the possibility of entrance of blood vessels from the peripheral fragment through the fracture line to the central fragment.

The nutrition of the central fragment, of course, plays the greatest role for the healing of the fracture and the nutrition of the head of the femur. Theoretically, recumbency for eight weeks without traction should furnish good conditions for such vascularization. Further, the patients as a rule are not harmed by this recumbency. They can move fairly freely in bed and generally require several weeks to obtain mobility of the extremities. After eight weeks' exercise in bed, the mobility generally is very good and the patient may walk relatively well shortly after having been allowed up.

IV. RESULTS

The material is compiled in Table III which comprises all cases admitted into and treated on the Third Surgical Service from March 15, 1935, to Dec. 31, 1937. Roentgenograms of every nailed medial fracture are reproduced in Figs. 13-21. In one case only (Case 33), the x-ray plate was lost. The clinical result in this case is excellent.

The general postoperative reaction has been remarkably slight; in no case threatening. As a rule rises in temperature and pulse have been minimal. Healing of the wound has occurred without serious complications in all of the 117 cases of nailing. In no single case has infection occurred around the nail. In 2 cases only a small hematoma occurred in the subcutaneous layer, 1 of which became injected. After drainage, both these wounds closed with a linear scar.

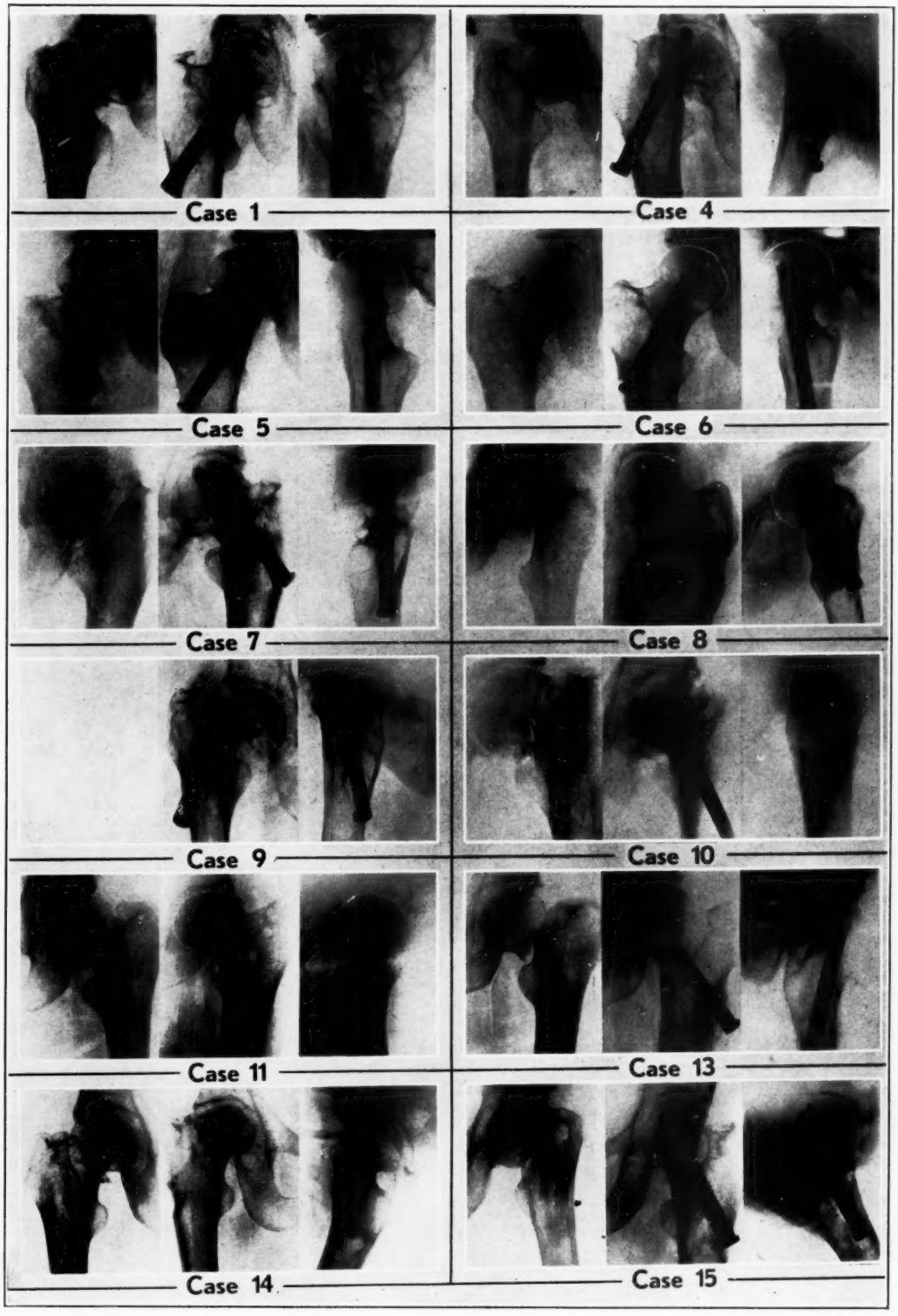

Fig. 13.

Figs. 13-21 (pages 339-347).—Three films of each case. The first presents the fracture before treatment; the second and third, the two last x-rays.

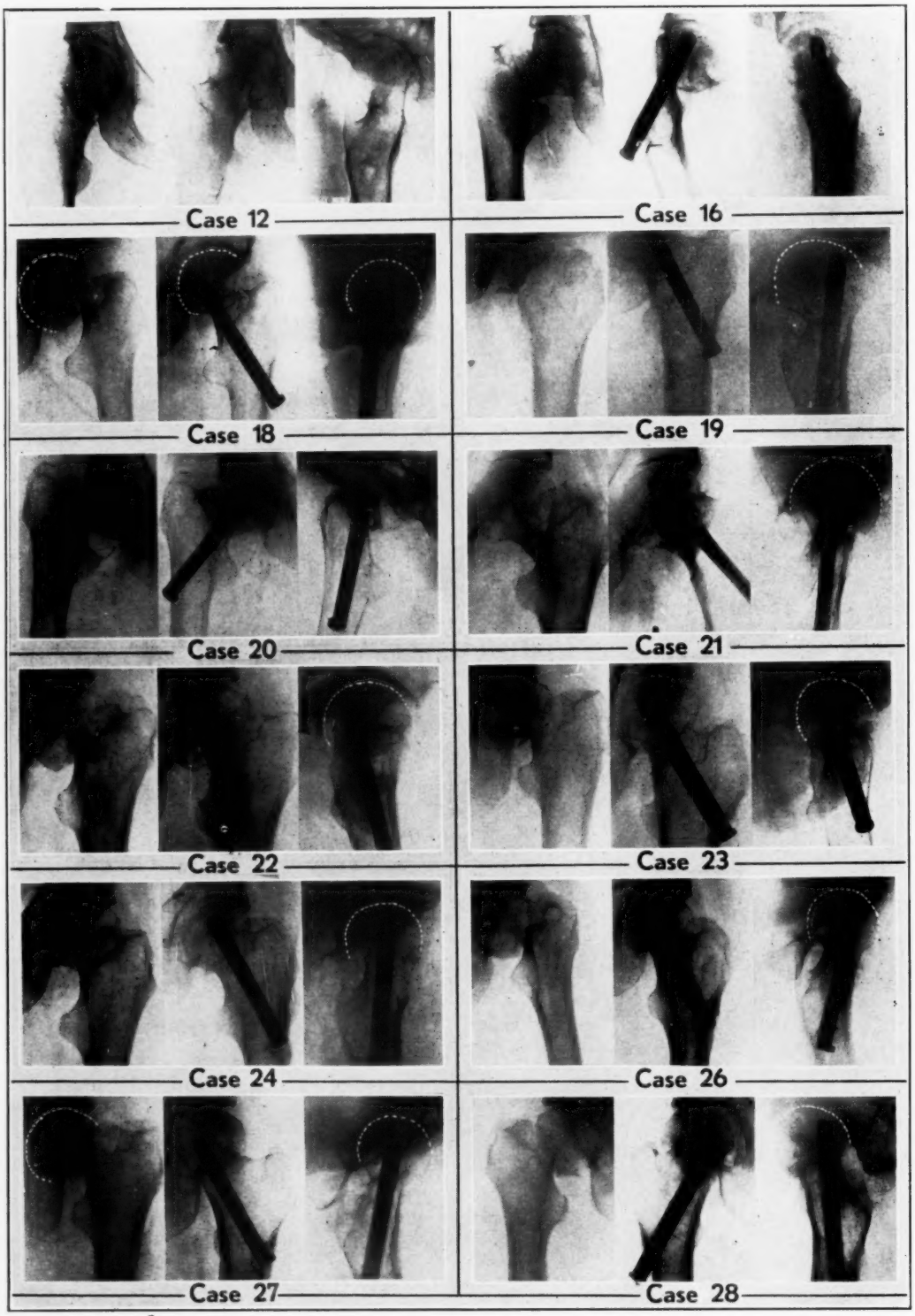
Case 12
Case 16
Case 18
Case 19
Case 20
Case 21
Case 22
Case 23
Case 24
Case 26
Case 27
Case 28

Fig. 14.

Case 29
Case 30
Case 32
Case 34
Case 35
Case 37
Case 38
Case 39
Case 40
Case 42
Case 43
Case 44

Fig. 15.

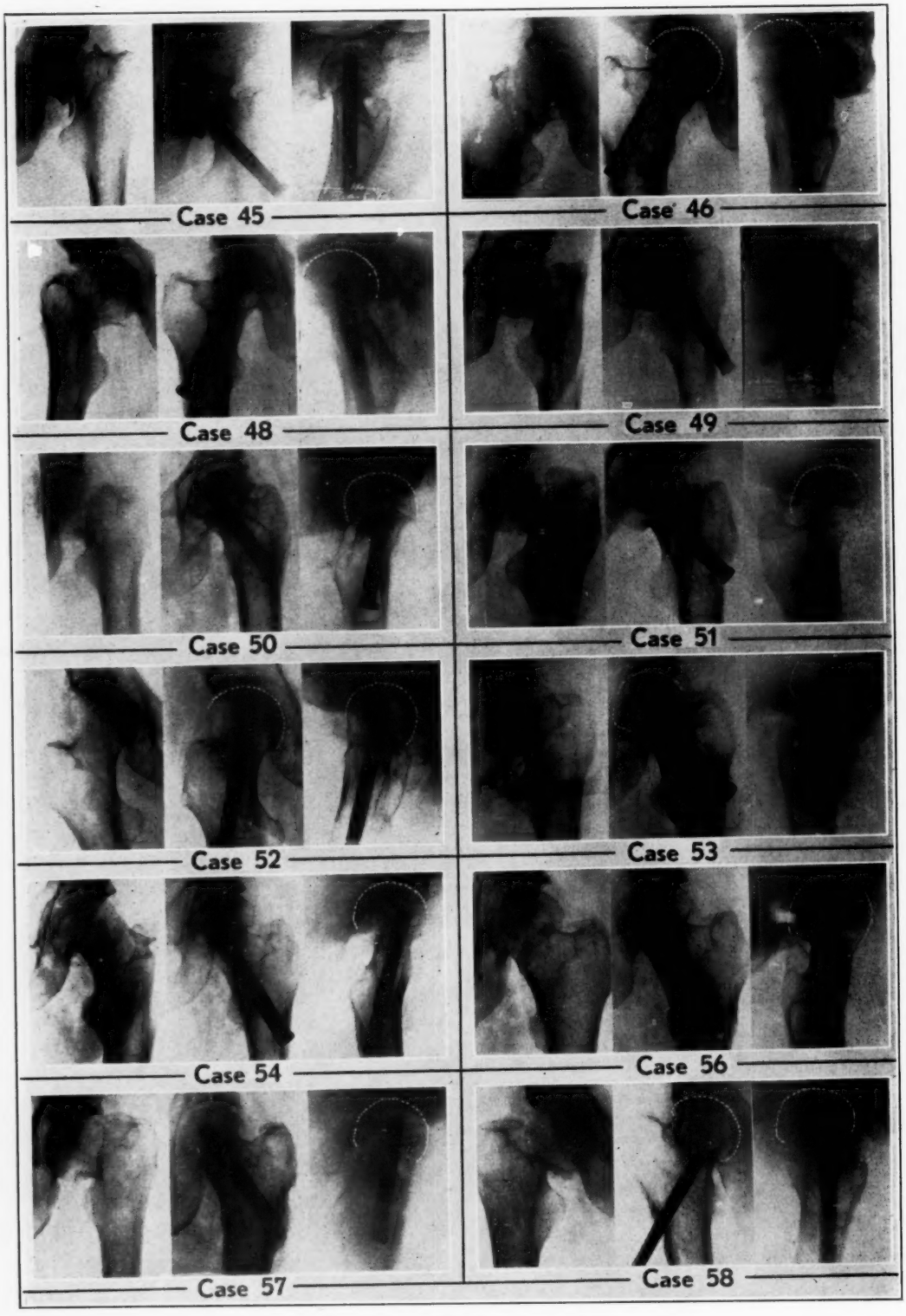
Case 45
Case 46
Case 48
Case 49
Case 50
Case 51
Case 52
Case 53
Case 54
Case 56
Case 57
Case 58

Fig. 16.

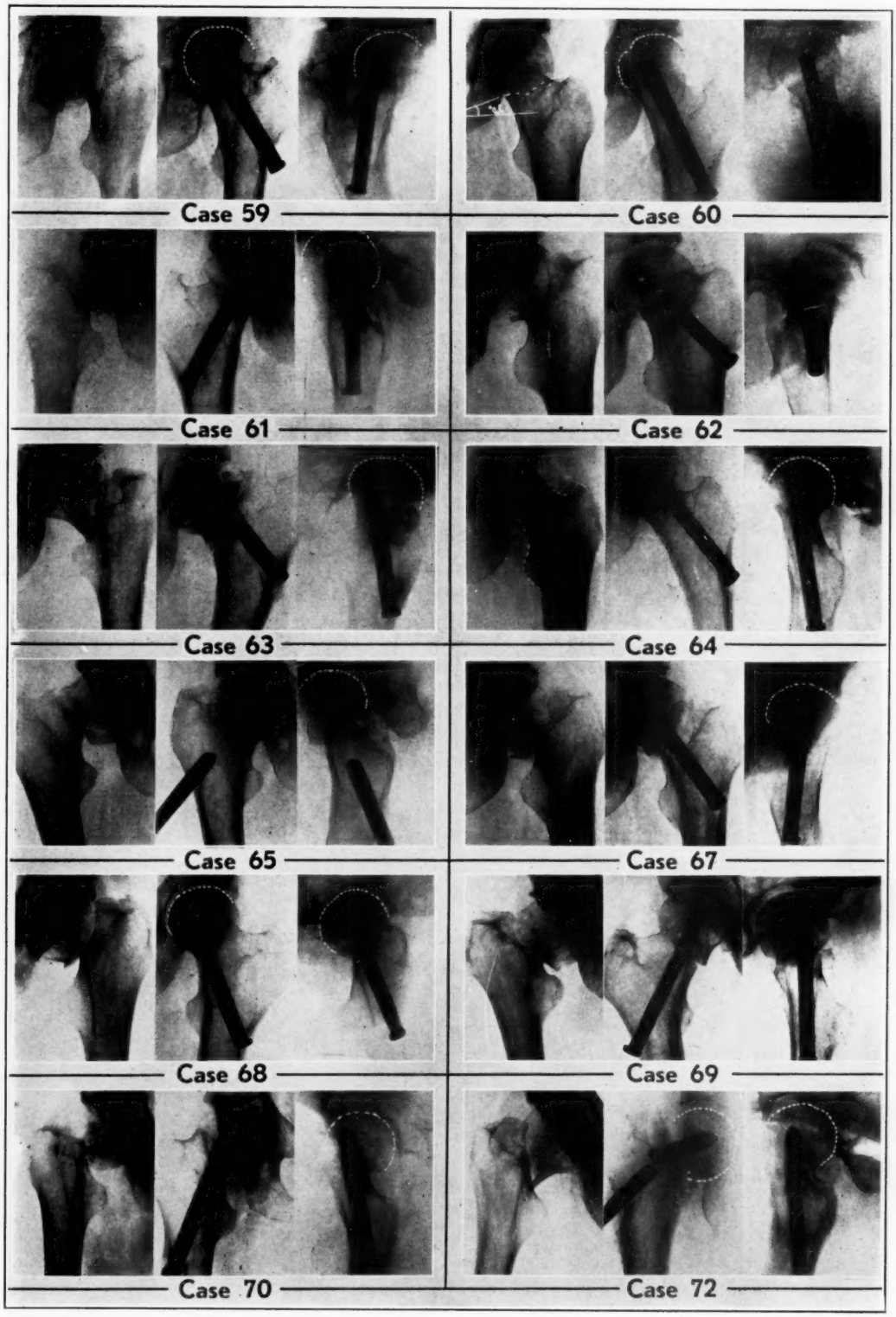
Case 59
Case 60
Case 61
Case 62
Case 63
Case 64
Case 65
Case 67
Case 68
Case 69
Case 70
Case 72

Fig. 17.

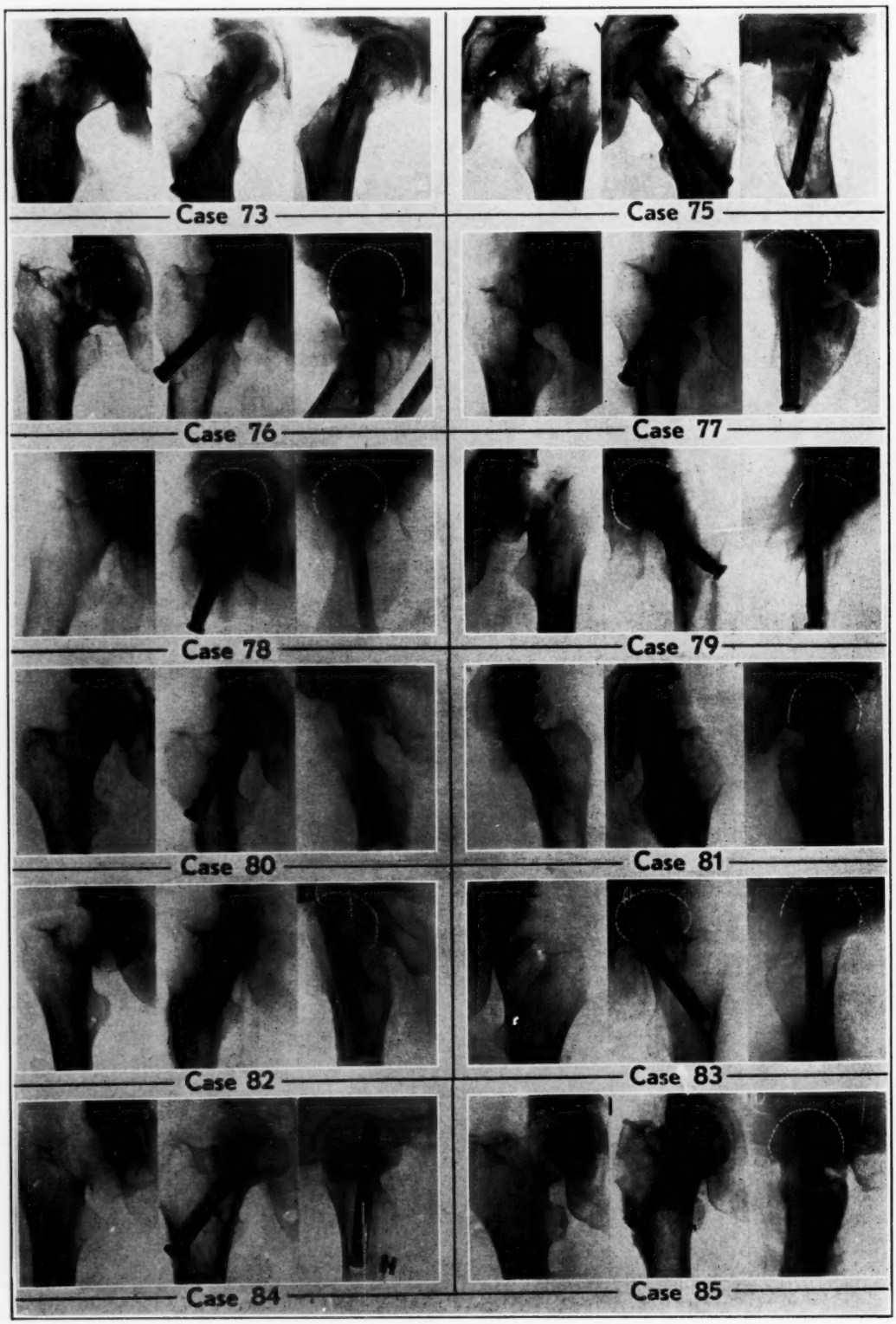
Case 73
Case 75
Case 76
Case 77
Case 78
Case 79
Case 80
Case 81
Case 82
Case 83
Case 84
Case 85

Fig. 18.

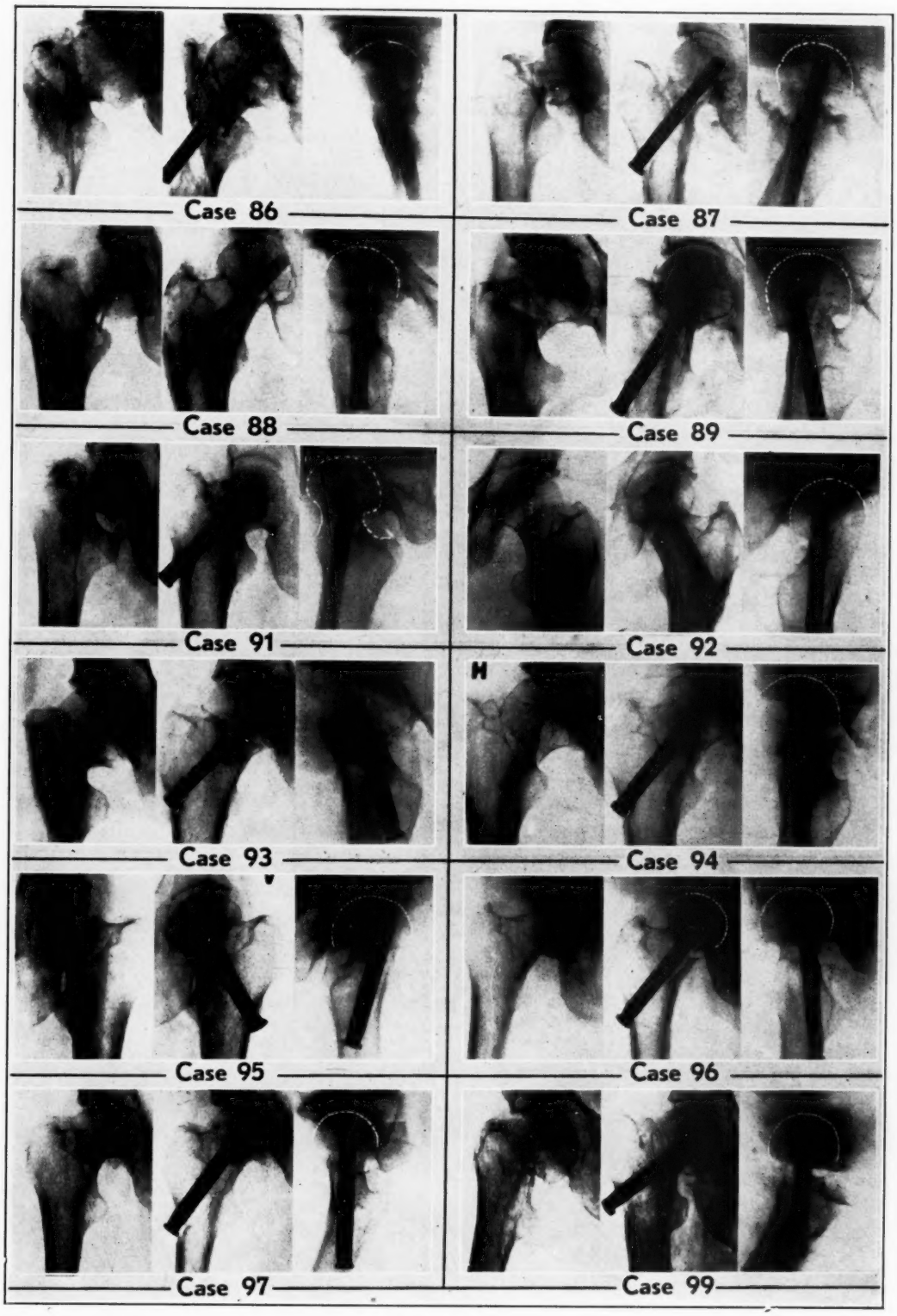
Case 86
Case 87
Case 88
Case 89
Case 91
Case 92
Case 93
Case 94
Case 95
Case 96
Case 97
Case 99

Fig. 19.

Case 101
Case 102
Case 103
Case 104
Case 105
Case 106
Case 108
Case 109
Case 110
Case 111
Case 112

Fig. 20.

These excellent results show that it is practicable to perform this operation with the patient in bed without risk of infection. They also demonstrate that drainage is not necessary in this operation. It has not been applied in any of these cases.

In 1 case in which "wire nailing" was performed and where the wire had been left protruding from the skin ("percutaneous wire nailing"), infection occurred. This method is not used now on the Third Surgical Service just because of the risk of infection.

Thrombosis and embolism have occurred in a total of 9 cases of 117 nailings, of 100 medial fractures in 7 cases, and of 17 lateral fractures

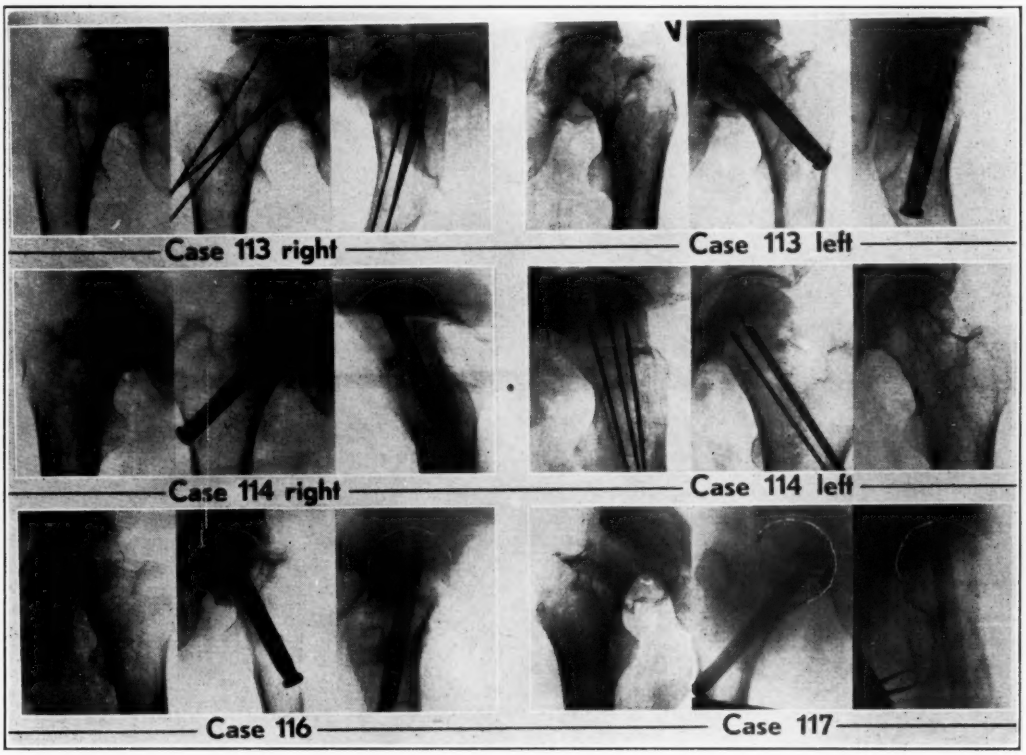

Fig. 21.

in 2 cases. The majority were slight cases which did not seriously affect the general condition. In no case has this complication been fatal.

These figures are surely not greater than those obtained with other methods of treatment of fractures of the femoral neck, quite probably smaller.

MORTALITY

Of 100 nailed medial fractures, 4 cases died within two months after the operation (4 per cent), 3 from bronchopneumonia (Cases 19, 97, 103) and 1 from apoplexy (Case 38). All patients were so ill before the operation that it is highly probable they would have died irrespective of

any treatment they might have received. It is hardly reasonable, therefore, to look upon these deaths as resulting from the operation. One patient died after discharge from the hospital.

This very modest mortality is remarkable for the reason that relatively so many of the patients have been very ill at the time they were nailed. As will appear from the "indications" (see p. 324), 84 per cent and 89 per cent respectively of all medial fractures have been operated upon.

The age of the patients is tabulated in Table II, from which it will be seen that 51 of the patients were more than 70 years of age.

Of 17 nailed lateral fractures, 2 died within two months after the operation, Case 2 from debility (76 years of age), Case 107 from bronchopneumonia (83 years of age). Both were very ill before the operation. One patient died later. These cases cannot be regarded, however, as straight cases of postoperative death.

The relatively low mortality after this operation (6 cases of 117 within two months [5 per cent]) indicates that it is a gentle intervention which is tolerated fairly well by these aged, and frequently very ill, patients.

THE FATE OF THE NAIL

The nail has a tendency to be extruded after a shorter or longer period. Chiseling off of the outer bone lamella of the femur corresponding to the point of introduction of the nail favors such extrusion.

At first (in 1935), when no provisions had been made to affix the nail, it slipped relatively often. In 4 cases the nail slipped out before bony union of the fracture had taken place. In 2 of these cases pseudarthrosis was the result, while the other 2 healed after the nail had been driven in again. In 5 cases the nail was extruded after bony union of the fracture had taken place. The slipping did not then disturb the bony union.

After a special technique had been adopted on the Third Surgical Service to prevent such extrusion, i.e., by driving the lower edge of the nail head inside the edge of the femur, a short slipping has occurred in only 3 cases out of about 95 nailings. This did not, however, have any detrimental effect on the fracture.

The objection has been raised against peripheral fixation of the nail that complications might occur if the neck of the femur were absorbed. The nail then would either penetrate into the joint or it would prevent the fracture surfaces from remaining in contact with each other.

In our material a slight absorption or shortening of the femoral neck has occurred in 9 cases. This corresponds to the so-called primary shortening due to defect at the fracture line. In only 1 case has the nail penetrated 1 to 2 mm. into the joint; this, however, happened because the nail was originally too long, placed immediately under the cartilage. In our material separation of the fracture surfaces as a consequence of the absorption has not occurred, even to a slight degree. This complication, therefore, plays no appreciable role.

Our material shows that it is justifiable and favorable to affix the nail to the edge of the femur by the technique mentioned. It furnishes an effective safeguard against extrusion, which is the chief precaution necessary. If the femoral neck becomes absorbed (shortened), the nail penetrates inward to a corresponding degree. The nail therefore, should not, be driven in more than to within 5 to 8 mm. from the joint surface. Greater shortening of the neck of the femur has not been observed in our material. The danger of penetration into the joint is then negligible.

Our late results prove that the nail head becomes covered by callus. This is favorable also because it protects the soft parts against irritation from the nail. If the nail head protrudes into the soft parts, this may cause formation of a tender, painful bursa, and this may be avoided by using the technique described.

In 3 cases the nail has broken out of the femoral head due to eccentric localization of the nail (Cases 13, 50, and 87). All these cases were renailed with good results.

In 1 case the nail was broken across eight months after the nailing, due to a manufacturing fault in the material. The patient is still under treatment, the fracture fixed by "wire nailing."

HEALING OF THE FRACTURE

As far as the medial fractures are concerned, usually about one year's observation is required to decide the question of bony union. In our material 55 cases have been controlled roentgenographically after a sufficiently long period of observation. Three cases showed deficient union; 2 cases were definite failures; 1 case, doubtful. In an additional 9 cases the patients have written to the effect that they had entirely recovered.

Of 64 cases, 2 (3?) were failures (i.e., less than 5 per cent). As to the remaining cases, the period of observation so far is too short to allow a statement.

The cause of difficulty in these 2 (3?) unsuccessful cases is extrusion of the nail due to a poor grip in 2 of the cases. In the third case, which may improve yet, the cause is delayed union due to inaccurate reduction. In all 3 cases technical errors seem to be chiefly responsible.

Slight absorption (shortening) of the femoral neck is found in 9 cases. In all of these the absorption was slight, from 2 to 5 mm., and played a negligible practical role. According to the roentgenograms in 5 of these cases, the cause seemed to be deficient reduction, particularly deficient impaction at operation, the fracture surfaces being held somewhat apart in their lowest part, or partly the result of a primary defect caused by the fracture itself. In only 1 case was no special cause discoverable.

TABLE III

100 CASES OF MEDIAL FRACTURES—NAILED

CASE NO.	AGE SEX	HOSPITAL DAYS	PREOPERATIVE COMPLICATIONS	OPERATION	POSTOPERATIVE COMPLAINT	FOLLOW-UP EXAMINATION												
						DATE	GAIT*	PAIN‡	ABLE TO WORK‡	RANGE OF MOTION (DEGREES)**					LAST X-RAY		CLINICAL RESULTS
										FLEXION	ABDUCTION	ADDUCTION	EXTERNAL ROTATION	INTERNAL ROTATION	DATE OF LAST X-RAY (UNION?)	POSITION OF NAIL	
1	76 F	7/18/35 to 9/ 5/35	Old fracture of the neck of the femur on the opposite side	7/25/35	0	6/30/37	II	+ –	+	75° (75)	45° (45)	45° (45)	90° (60)	0° (0)	6/30/37 Bony	Unchanged	Cured
4	87 F	3/17/35 to 5/ 7/35	0	3/25/35	0	12/17/35 (Letter July, 1937)	II	+ –	+	40° (120)	5° (15)	20° (50)	0° (40)	0° (60)	12/17/35	Nail slipped 2 cm.; reintroduced	Cured
5	49 F	4/24/35 to 6/15/35	Ankle edema	4/30/35	Slight thrombosis	9/21/37	I	+ –	+	N	N	N	N	10° (25)	9/21/37 Bony	Unchanged	Cured
6	59 F	6/15/35 to 8/28/35	0	6/19/35	Slight thrombosis	6/28/37	I	–	+	N	N	N	N	N	6/28/37 Bony	Unchanged	Cured
7	64 M	7/ 5/35 to 8/30/35	Cerebral syphilis, spinal tabes	7/18/35	0	9/ 3/37	II	+	–	80° (90)	N	N	45° (60)	10° (15)	9/3/37 Bony	Unchanged	Cured
8	70 F	6/ 7/35 to 8/31/35	0	6/19/35	0	11/25/37	II	–	+	60° (100)	15° (20)	30° (45)	45° (30)	0° (30)	11/25/37 Bony	Unchanged	Cured
9	72 F	3/20/35 to 6/ 8/35	Renal pathology, knee injury, senility	4/ 8/35	Peroneal palsy	6/ 2/36	III-IV	+ –	–						10/2/36 Nonunion	Nail slipped after 8 mon.	Poor
10	58 M	4/ 4/35 to 6/ 7/35	6 months old fracture	5/ 7/35	0	11/ 8/37	II	+ –	+	80° (100)	N	N	45° (80)	10° (30)	10/26/37 Bony	Nail slipped after 2 yr.	Cured
11	78 F	6/23/35 to 9/ 7/35	0	7/25/35	0	12/ 6/37	II-III	+	–	N	45° (50)	30° (40)	20° (45)	0° (10)	12/6/37 Bony	Nail slipped after 1½ yr.	Improved
12	59 F	2/ 7/35 to 4/17/35	0	2/12/35	0	9/10/36	I	–	+	N	N	N	N	Slightly reduced	9/10/36 Bony	Slipped after 1 yr.; removed	Cured

*I—indicates a perfect gait, which cannot be criticized in any way; II—indicates a very good gait, with negligible discomfort of one kind or another; III and IV—indicate poor gait or recumbency, respectively.

†N—normal.

‡ + —indicates pain; – —no pain; + - —slight, inconstant pain.

** ( ) —indicate motion of the other hip joint.

TABLE III.—CONT'D

13	68 F	4/24/36 to 9/12/36	0	5/ 4/36	0	6/30/37	II	+ –	+	90° (100)	N	N	N	N	7/5/37 Bony	Nail broken posteriorly through; reoperation	Cured
14	70 F	7/ 1/36 to 9/23/36	Fracture of the neck humerus	7/21/36	0	9/1/37	II	+	–	85° (90)	45° (50)	N	N	10° (30)	9/1/37 Bony	1 to 2 mm. too long after shortening at the neck; removed	Improved
15	78 F	9/27/35 to 12/18/35	0	10/10/35	0	11/22/37 (letter)	I	–	+							Slipped after 1 mon.; reintroduced	Cured
16	82 F	7/26/35 to 9/ 4/35 9/21/35 to 11/18/35	0	7/29/35	0	6/29/37	II	+	–	N	N	N	N	Reduced	6/29/37 Bony	Slipped; reintroduced after 2½ mon.	Cured
18	77 F	9/15/35 to 11/23/35	Hemiplegia, nephrolithiasis, sciatica	10/11/35	0	11/16/37	IV	–	–	65° (90)	N	N	N	10° (10)	7/21/37 Bony	Unchanged	Improved
19	78 F	9/17/35 to 10/13/35	Apoplexia, debility	10/ 1/35	Bronchopneumonia	10/12/35 (death)		–									
20	85 F	4/17/35 to 6/15/35	Arthritis	4/24/35	0	11/16/37 (letter)	II	–	+						6/15/35 ?		Cured
21	81 M	11/ 2/35 to 1/27/36	Vertigo	1/18/36	0	7/ 9/37	II	–	–	85° (110)	N	N	45° (60)	N	7/9/37 Bony	Unchanged	Cured
22	60 M	6/27/35 to 7/26/35	Alcoholism delusions	7/ 5/35	0	9/25/37 (letter)	II	–	–						11/11/35 ?	Unchanged	Cured
23	68 F	6/ 3/35 to 7/29/35	Uterine prolapse	6/12/35	0	11/18/35 9/11/37 (letter)	I I	– –	– –	N	N	25°	N	20°	11/18/35 ?	Unchanged	Cured
24	79 F	12/14/35 to 2/18/36	0	12/21/35		9/ 3/36	I	–	+	N	N	N	N	5°	9/3/36 Bony	Unchanged	Cured
26	62 F	11/25/35 to 2/28/36	0	12/30/35	0	11/17/37	I	–	+	N	N	N	N	N	11/17/37 Bony	Unchanged	Cured

TABLE III.—CONT'D

CASE NO.	AGE SEX	HOSPITAL DAYS	PREOPERATIVE COMPLICATIONS	OPERATION	POSTOPERATIVE COMPLAINT	FOLLOW-UP EXAMINATION												
						DATE	GAIT*	PAIN‡	ABLE TO WORK‡	RANGE OF MOTION (DEGREES)**					LAST X-RAY		CLINICAL RESULTS
										FLEXION	ABDUCTION	ADDUCTION	EXTERNAL ROTATION	INTERNAL ROTATION	DATE OF LAST X-RAY (UNION?)	POSITION OF NAIL	
27	64 F	1/28/36 to 3/ 9/36	0	2/17/36	6 days postoperative cerebral apoplexy	11/15/37	In bed IV (apoplexy)	−	−		Greatly reduced				11/18/37 Bony	Unchanged	Cured
28	74 F	12/23/35 to 3/11/36	Fracture of radius	12/30/36	0	6/30/37		+	+	135° (145)	N	N	N	N	7/8/37 Bony	Unchanged	Cured
29	57 F	12/26/35 to 3/17/36	0	1/ 7/36	0	7/14/37	I	+	+	100° (110)	50° (60)	N	N	N	7/14/37 Bony	Unchanged	Cured
30	71 F	1/10/36 to 3/18/36	Fracture of humeri	1/17/36	0	11/17/37 (per telephone)	I	−	+						9/2/36 Bony	Unchanged	Cured
32	46 M	1/15/36 to 3/23/36	0	1/16/36	0	July, 1937	I	+ −	+	100° (110)	N	N	N	N	9/7/36 Bony	Unchanged	Cured
33	53 F	1/ 2/36 to 5/20/36	0	1/ 7/36 and 2/13/36	Embolism	7/ 2/37	II	+ −	+	90° (110)	60° (95)	N	N	5° (15)	7/2/37 Bony	Unchanged	Cured
34	57 F	3/31/36 to 7/ 6/36	Heart disease; fracture of forearm	4/23/36	0	7/19/37	II	+	+ −	90°	60°	40°	30°	30°	7/19/37 Bony	Unchanged	Cured
35	79 F	3/21/36 to 6/ 8/36	0	3/27/36	0	9/ 7/37	II	−	−	50°	20°	10°	N	N	9/7/37 Bony (?)	Unchanged, shortening of neck	Improved
37	70 M	7/25/36 to 9/22/36	Insanity	8/24/36	0	6/28/37	II	−	+	N	N	N	N	15°	6/28/37 Bony	Unchanged	Cured
38	73 F	9/24/36 to 11/ 1/36	Debility	9/30/36	1/11/36 Hemorrhagia cerebelli bronchopneumonia; death												

TABLE III.—CONT'D

39	63 M	9/10/36 to 11/23/36	Pes equino varus congenita bilateral	9/17/36	0	8/26/37	I	−	+	N	N	N	N	N	8/26/37 Bony	Unchanged	Cured
40	72 M	8/ 8/36 to 10/24/36	Hernia 0	8/18/36	0	8/18/37	I	−	+	N	N	N	N	5° (10/15)	1/26/37 Bony	Unchanged	Cured
42	63 M	9/ 8/36 to 12/ 5/36	0	9/14/36	0	8/24/37	II	+	−	N	N	N	N	N	8/24/37 Bony	Unchanged	Cured
43	80 F	3/26/36 to 4/30/36	Neuralgia	4/ 1/36	0	9/ 8/36 12/ 1/37	II I	− −	− −	90°	30°	30°	5°	0°	9/8/36 Bony	Unchanged	Cured
44	54 F	2/24/36 to 5/ 2/36	Fracture of lower leg	2/29/36	0	7/ 1/37	I	+	+	105° (110)	N	30° (45)	45° (60)	N	7/1/37 Bony	Unchanged	Cured
45	77 F	2/ 5/36 to 5/ 2/36	0	2/12/36	0	9/ 6/37	I	−	+	N	N	N	N	N	9/7/36 Bony	Unchanged	Cured
46	68 F	2/10/36 to 5/ 4/36	933: fracture of the medial condyle of tibia	2/22/36	0	7/ 7/37	II	−	+	N	N	N	60° (75)	45° (60)	7/14/37 Bony	Unchanged	Cured
48	43 F	1/21/36 to 5/ 7/36	Thrombosis 0	3/ 5/36	0	7/ 8/37	I-II	+ −	+	N	N	N	N	N	7/7/37 Bony	Unchanged	Cured
49	70 F	11/11/35 to 5/13/36	Arteriosclerosis, fractured radii	11/29/35	0	9/ 4/36 July, 1937	III III-IV	+ + +	+ −	N	20° (30)		0°	0°	9/4/36 Nonunion	Nail slipped; reintroduced	Poor
50	76 F	2/16/36 to 5/13/36	Knee injury, shortening 2	2/22/36 and 4/15/36	0	10/ 5/37	II (?) II	+ −	+ −	N	45° (50)	N	45° (80)	40° (80)	10/5/37 Bony-incipient necrosis (?)	Nail broken through; renailed	Improved
51	62 F	1/27/36 to 4/ 8/36	Fracture of radius Albuminuria	2/ 8/36	0	9/15/37 (per post)	II	+	−						2/21/36 (?)	Unchanged	Cured
52	79 F	3/ 5/36 to 5/14/36	Debility	3/12/36	0	9/11/36	II		−	90°	30°	30°	30°	5°	9/11/36 Bony	Unchanged	Cured
53	62 F	3/ 8/36 to 5/19/36	Fracture malleolar lateral (1929), intestinal complaints, debility	3/18/36	0	1/ 4/38	II	+ −	−	110° (120)	30° (45)	N 30° (30)	25° (30)	5° (5)	1/4/37 Bony	Unchanged	Cured

TABLE III.—CONT'D

CASE NO.	AGE SEX	HOSPITAL DAYS	PREOPERATIVE COMPLICATIONS	OPERATION	POST-OPERATIVE COMPLAINT	FOLLOW-UP EXAMINATION											CLINICAL RESULTS
						DATE	GAIT*	PAIN‡	ABLE TO WORK‡	RANGE OF MOTION (DEGREES)**					LAST X-RAY		
										FLEXION	ABDUCTION	ADDUCTION	EXTERNAL ROTATION	INTERNAL ROTATION	DATE OF LAST X-RAY (UNION?)	POSITION OF NAIL	
54	73 F	4/30/36 to 7/ 9/36	Fracture of arm (1917), arthritis	6/ 2/36	0	12/14/37	I	+	−	N	45° (50)	40° (50)	30° (50)	20° (30)	12/14/37 Bony	Unchanged	Cured
56	75 F	10/13/36 to 12/31/36	0	12/21/36	0	7/ 9/37	II	+ −	+	90° (100)	N	N	N	N	7/9/37 Bony	Unchanged	Cured
57	72 F	8/ 1/36 to 10/16/36	0	8/13/36	0	11/29/37	I	−	+	N	N	N	N	N	11/29/37 Bony	Unchanged	Cured
58	63 F	1/27/36 to 3/25/36	Arthritis	2/10/36	0	8/30/37	II	+ −	+	60° (90)	30° (60)	20°	15° (30)	10°	8/30/37 Bony, slight shortening of the neck	Nail slipped; removed after 9 mo.	Cured
59	85 F	1/14/36 to 3/28/36	Arthritis	1/20/36	Thrombosis	11/18/37	I	−	+	N	N	N	N	N	11/18/37 Bony	Unchanged	Cured
60	33 F	2/ 1/36 to 3/28/36	0	2/ 5/36	0	July, 1937	I	−	+	N	N	N	N	N	9/4/36 Bony	Unchanged	Cured
61	58 F	12/20/35 to 3/30/36	0	1/ 2/36	Pulmonary embolism	7/ 1/37	I	−	+	N	N	N	N	N	7/1/37 Bony	Unchanged	Cured
62	60 M	1/22/36 to 4/ 4/36	9	2/ 6/36	Pulmonary embolism	12/ 8/37	I	−	+	N	N	N	N	N	12/8/37 Bony	Unchanged	Cured
63	58 F	2/ 5/36 to 4/11/36	Dyspepsia	2/10/36	0	July, 1937	II	+	+ −	N	15°	N	N	N	12/1/37 Slight shortening of neck; union (?)	Unchanged	Improved
64	72 F	2/ 5/36 to 4/25/36	0	2/17/36	0	6/29/37	I-II	+	+	90°	N	N	N	Reduced	6/29/37 Bony	Unchanged	Cured
65	50 F	2/20/36 to 4/30/36	0	2/29/36	0	10/13/37	I	−	+	90°	N	N	N	N	10/14/37 Bony	Nail slipped; removed 10/18/37	Cured

TABLE III.—CONT'D

67	66 F	11/23/36 to 2/ 5/37	Fracture of radius	12/ 3/36	0	July, 1937	II	–	+	95° (105)	30° (60)	N	N	45° (60)	2/1/37 ?	Unchanged	Cured
68	53 F	12/ 6/36 to 2/18/37	Tuberculosis of foot, eczema	12/17/36	0	8/28/37 (letter by mail)	I	–	+						2/18/37 ?	Unchanged	Cured
69	47 F	7/12/36 to 2/20/37	0	12/16/36	0	2/20/37	II	+ –	–	100°	25°	35°	20°	25°	2/20/37 ?	Unchanged	?
70	70 F	11/ 7/36 to 2/27/37	0	12/16/36	0	9/10/37	II	–	Old age, too old	90° (100)	N	N	N	N	9/10/37 ?	Unchanged	Cured
72	66 F	1/15/37 to 3/24/37	Dyspnea	1/28/37	0	6/ 9/37 9/ 1/37	II III-IV	+ +	–	90°	45°		30°	15°	12/16/37 ?	Nail broken; removed; fixation by wires	Poor (?)
73	14 F	5/ 3/37 to 5/21/37	0	3/22/37	0	8/ ?/37	I-II	–	+	N	N	N	N	N	8/19/37 Bony	Unchanged	Cured
75	46 M	4/ 8/37 to 6/ 1/37	0	4/20/37	0	7/15/37	II	–	–	45° (90)	?	?	?	?	7/15/37 ?	Unchanged	Improved
76	57 M	4/25/37 to 6/ 5/37	Urinary complaints	4/30/37	0	8/20/37 (letter by mail)	II	+	–						6/1/37 ?	Unchanged	Improved
77	70 F	3/22/37 to 6/ 8/37	0	3/29/37	Ankle edema	9/28/37	II	+	–	70° (80)	45° (50)	45° (50)	45° (90)	50° (60)	9/28/37 Slight shortening of neck	Unchanged	Improved
78	72 F	4/27/37 to 6/ 8/37	Vertigo, epilepsia	5/13/37	0	8/26/37 (dead)			–						5/27/37	Unchanged	
79	83 F	1/ 2/37 to 3/ 8/37	Fracture of radii	1/ 9/37	0	9/23/37	III	+	–	90° (100)	30° (40)	10° (45)	5° (45)	15° (45)	9/23/37	Nail too long to be removed	Improved
80	84 F	12/13/36 to 2/14/37	Arteriosclerosis	12/17/36	0	5/29/37 (letter by mail) 11/13/37)	I-II I	–	+	N	N	N	N	N	2/13/37	Unchanged	Cured
81	69 F	1/10/37 to 3/24/37	0	1/27/37	Knee injuries	11/17/37	II	In the knee	+ –	N	N	N	N	N	11/17/37 Bony	Unchanged	Cured
82	66 F	12/ 9/36 to 2/19/37	0	12/17/36	0	7/ 2/37	I	–	+	N	N	N	N	15° (60)	7/2/37 Bony	Unchanged	Cured

TABLE III.—CONT'D

CASE NO.	AGE SEX	HOSPITAL DAYS	PREOPERATIVE COMPLICATIONS	OPERATION	POST-OPERATIVE COMPLAINT	FOLLOW-UP EXAMINATION												
						DATE	GAIT*	PAIN‡	ABLE TO WORK‡	RANGE OF MOTION (DEGREES)**					LAST X-RAY		CLINICAL RESULTS
										FLEXION	ABDUCTION	ADDUCTION	EXTERNAL ROTATION	INTERNAL ROTATION	DATE OF LAST X-RAY (UNION?)	POSITION OF NAIL	
83	55 F	1/10/37 to 3/13/37	Neuralgia	1/11/37	0	July, 1937	II	+	−	90° (150)	N	N	45° (60)	20° (25)	10/19/37 Bony	Unchanged	Cured
84	69 F	1/15/37 to 3/30/37	0	1/23/37	0	8/25/37	II	−	+ −	N	N	N	N	N	8/25/37 Bony	Unchanged	Cured
85	63 F	1/12/37 to 3/19/37	0	1/19/37	0	11/ 2/37	II	−	−	N	N	N	N	N	11/2/37 3 mm. shortening of neck (?)	3 mm. inward	Cured
86	86 M	12/24/36 to 1/16/37	Diabetes, heart disease, debility	1/ 6/37	0	11/13/37 (by telephone)	III-IV	+	−						6/10/37 ?	Unchanged	Improved
87	71 F	12/ 6/36 to 4/26/37	Diabetes	12/31/36	0	7/26/37	III	+	−	75° (115)	30° (60)	Slightly reduced	N	N	7/26/37 ?	Nail broken through; renailing Unchanged	Improved
88	63 F	10/24/36 to 1/16/37	0	10/28/36	Slight thrombosis	10/ 8/37	II	+	−	90° (100)	40° (45)	30° (45)	N	N	10/8/37 Bony	Unchanged	Cured
89	73 M	10/26/36 to 1/23/37	0	11/9/36	0	9/ 9/37	II	+	−	80° (90)	40° (50)	N	N	5° (10)	9/9/37 Bony	Nail slipped ½ cm. outward	Cured
91	79 F	12/23/36 to 2/26/37	0	12/29/36	0	8/ 3/37	II	+ −	+	?	Slightly reduced	N	25° (35)	20° (60)	8/3/37 ½ cm. shortening of neck	Nail ½ cm. out	Cured
92	52 F	12/23/36 to 3/ 3/37	0	1/ 4/37	0	6/28/37	II	−	+	Slightly reduced (3 to 5°)	N	N	N	45° (60-70)	6/28/37 Bony	Unchanged	Cured
93	63 M	1/ 4/37 to 3/ 6/37	0	1/15/37	0	6/23/37	II	+ −	−	N	N	N	N	N	6/29/37 ?	Unchanged	Cured

TABLE III.—CONT'D

94	39 M	3/ 6/37 to 4/30/37	0	3/19/37	0	7/27/37	I	−	+	N	N	N	N	N	7/27/37 ?	Unchanged	Cured
95	82 F	2/14/37 to 5/ 3/37	0	2/27/37	0	9/16/37	II	−	+ −	N	N	N	N	N	9/16/37 2 mm. shortening of the neck	Nail 2 mm. inward	Cured
96	72 F	5/29/37 to 6/22/37	Diabetes	6/11/37	Apoplexy 8/8/37	11/15/37	IV	?	In bed −			Reduced			8/5/37	Unchanged	?
97	69 F	5/19/37 to 6/22/37	Debility	5/25/37	Bronchopneumonia; death 7/6/37										6/1/37	Unchanged	?
99	81 F	6/10/37 to 7/10/37	Debility	6/15/37	0	9/22/37	II	+	−	N	N	N	N	N	8/12/37 Slight shortening of the neck	Unchanged	?
101	65 F	6/16/37 to 7/22/37		6/26/37	0	9/10/37	II	−	+	N	N	N	N	N	8/10/37 ?	Unchanged	?
102	75 F	6/12/37 to 7/12/37	0	7/ 1/37	0	8/27/37	II	+ −		N	N	N	N	N	8/11/37	Unchanged	?
103	80 F	5/15/37 to 5/27/37	Disoriented, debility	5/21/37	Bronchopneumonia; death 6/8/37										5/25/37		
104	66 F	6/15/37 to 7/14/37	Asthma vititim cordis, arthritis	6/23/37	Embolism	9/ 7/37	III	+	−	N	45° (10)	40° (45)	N	N	8/5/37	Unchanged	?
105	71 M	7/ 3/37 to 8/12/37	Vertigo	7/ 7/37	0	8/24/37	II	−	−	90° (100)	50° (60)	N	N	N	8/24/37	Unchanged	?
106	63 F	8/30/37 to 9/29/37	Fracture of ankle 5 yr. ago	9/16/37	0	11/25/37	II	−	−						11/13/37	Unchanged	?
108	67 F	11/ 3/37 to 12/ 2/37	0	11/15/37	0	1/ 1/38	In bed	−							12/21/37	Unchanged	?

TABLE III.—CONT'D

CASE NO.	AGE SEX	HOSPITAL DAYS	PREOPERATIVE COMPLICATIONS	OPERATION	POSTOPERATIVE COMPLAINT	FOLLOW-UP EXAMINATION											
						DATE	GAIT*	PAIN‡	ABLE TO WORK‡	RANGE OF MOTION (DEGREES)**					LAST X-RAY		CLINICAL RESULTS
										FLEXION	ABDUCTION	ADDUCTION	EXTERNAL ROTATION	INTERNAL ROTATION	DATE OF LAST X-RAY (UNION?)	POSITION OF NAIL	
109	64 M	9/ 7/37 to 10/19/37	0	10/ 7/37	0	11/20/37	In bed	–							11/20/37	Unchanged	?
110	79 F	10/26/37 to 11/27/37	Apoplexy 3 yr. ago	11/11/37		12/ 4/37	In bed	–							11/18/37		?
111	82 F	10/19/37 to 11/17/37	Cerebral hemorrhage 7/15/37	11/ 4/37	0	11/17/37	In bed	–							12/28/37	Unchanged	?
112	78 F	11/ 6/37 to 12/ 7/37	0	11/8/37	0	12/ 7/37	In bed	–							12/28/37	Unchanged	?
113	74 F	11/14/37 to 12/ 2/37	Fracture of neck of femur on the opposite side 2 yr. ago.	11/19/37	0	12/ 2/37	In bed								1/4/38	Unchanged	Fracture on opposite side; complete cure, wire fixation
114	79 F	9/25/37 to 10/13/37	Fracture of neck of femur on opposite side 2 yr. ago	10/ 5/37	0	10/13/37	In bed								12/2/37	Unchanged	Fracture on opposite side cured by wire fixation
116	80 F	12/18/37 to 1/ 7/38	Debility, senility	12/21/37	0	1/ 1/38	In bed								12/28/37	Unchanged	?
117	75 F	11/18/37 to 1/11/38	0	12/ 1/37	0	1/ 1/38	In bed								12/1/37	Unchanged	?

Shortening of the femoral neck, therefore, sometimes appears to be the result of errors in technique, particularly with regard to the reduction. Our material demonstrates that an accurate reduction and good impaction generally prevent shortening of the neck of the femur. This complication, therefore, plays a quite subordinate part in our material.

Necrosis of the femoral head has been brought forward as an argument against nailing. The typical necrosis (one to two years after successful nailing) has not been demonstrated in a single case in our material.

In one case partial necrosis occurred after malposition of the fracture due to extrusion of the nail (Case 9). This was explained, however, as caused directly by the malposition, and the deficiency of nutrition of the femoral head resulting from this. In another case (Case 50) abundance of calcium in the head of the femur one and one-fourth years after nailing indicates deficient nutrition. Pronounced necrosis was not found, however.

The period of observation of the majority of our cases has been too brief to enable us to evaluate the incidence of this complication. According to our present experience, it appears to play a very subordinate role.

It is theoretically probable that the nutrition of the femoral head in some degree depends upon the nutrition from the peripheral fragment.

An accurate reduction and good immobilization of the fracture, for example, during eight weeks' recumbency without traction, should favor vascularization through the fracture line.

The good results obtained in our material by this procedure may support this possibility. Of the 17 nailed lateral fractures all the surviving patients obtained bony union within three to four months.

CLINICAL RESULTS

Pain in the leg is present, chiefly when there is unsuccessful union. With successful bony union, slight pain and slight discomfort are not unusual, but these are not particularly embarrassing (Table III). Ability to work has been recorded in the table. In these old patients it is of fairly subordinate consequence. The gait has been judged according to estimate: I indicates a perfect gait, which cannot be criticized in any way, and this is found in a total of 26 cases. II indicates a very good gait, with negligible discomfort of one kind or another, in a total of 51 cases. III and IV indicate poor gait or recumbency, respectively, in a total of 9 cases.

Of the total of 100 cases of medial fractures in our material 9 are still under treatment and 5 have died. Of the remaining 86 patients, 77 have excellent or good gait (90 per cent).

Regarding the end results, it is as yet too early to make any definite statement, because a considerable number of the cases has been observed for too short a time.

Of the total of 100 cases of medial fractures, 5 have died; 2 cases, possibly 3, have failed as to end results and the remainder are cured or improved.

Bilateral nailing of medial fractures has been performed in 2 cases (Case 113 and Case 114); i.e., "wire nailing" on one side and ordinary nailing on the other side. The results are good.

Of 17 lateral fractures, 3 have died; the remainder have been cured or improved.

SUMMARY

A simple and gentle method is presented for reducing and nailing fractures of the femoral neck. The reduction is performed with wire traction on a specially constructed splint, which permits extensive internal rotation. The result of the reduction is ideal in 98 per cent of the cases.

The traction treatment permits preliminary treatment of the patient prior to the operation and observation of the patient with a view to indication for and selection of a favorable time for nailing.

The leg is kept lying in unchanged position on a splint until after the nailing is completed. The nailing is carried out while traction is maintained and with the patient lying in bed under local anesthesia.

In order to ensure an accurate centering of the nail, a special sighting apparatus has been constructed for the aiming of the wire and the nail in two planes.

This procedure permits reduction as well as operation on very ill patients. Eighty-four to 89 per cent of all medial fractures have been so treated, a total of 100 operations in the course of three years. The results show that 2 per cent died within two months after the operation. Only 2 (3?) were failures as far as fixation of the fracture is concerned. Bilateral nailing was used in 2 cases. Of 38 lateral fractures, 17 were nailed by the same method. Two died within two months. Bony union occurred in all the surviving cases.

REFERENCES

1. Löfberg: Acta chir. Scandinav. **57:** 504, 1924.
2. Nicolaysen, J.: N. Med. Arkiv., 1897.
3. Schilling, Hj.: Personal communication, Forh. Nordisk Kir. Forening, Stockholm, 1931.
4. Smith-Petersen, M. N.: Arch. Surg. **23:** 715, 1931; Surg., Gynec. & Obst. **64:** 287, 1937.
5. Backer-Grøndahl, N.: Surg., Gynec. & Obst. **64:** 1073, 1937.
6. Johansson, S.: Zentralbl. f. Chir., **59:** 2019, 1932, Operative Treatment of Fractures of the Neck of the Femur, Kjøbenhavn, 1934, Levin & Munksgaard.
7. Pauwels: The Fracture of the Neck of the Femur. A Mechanical Problem, Leipzig, 1935, Georg Sturm.
8. Nystrøm, G.: Acta chir. Scandinav. **76:** 1, 1935.

THE RELIEF OF PAROXYSMAL HYPERTENSION BY EXCISION OF PHEOCHROMOCYTOMA

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INTRODUCTION

A NUMBER of reports of pheochromocytomas (paragangliomas) have now accumulated in the literature. The majority of the recorded cases were of post-mortem examinations. However, in recent years the clinical recognition of these neoplasms has been possible because of the realization of their causal relationship to paroxysmal hypertension. Vaquez and Donzelot were the first to diagnose such a tumor in vivo and this was not until 1926. A review of the clinical syndrome and of the histopathology of these neoplasms would be needless repetition here in view of the several adequate articles already published (Rabin, Belt and Powel).

On the other hand there is not a great deal of recorded operative experience in the treatment of these neoplasms nor have many studies on their adrenalin content been made. With the purpose of emphasizing these points, the following case is recorded.

CASE REPORT.—F. K. (No. 169122), white female, 41 years of age, admitted to the Medical Service of Dr. George F. Dick, March 28, 1937, complaining of "attacks" that are characterized as follows: A feeling of constriction in the head, then the chest which induces marked labored breathing; palpitation and tachycardia, pain in the midportion of the abdomen, nausea and often vomiting. By this time there is a sensation of marked weakness and then purposeless movements of the arms and legs, mostly on the right, which however can be voluntarily controlled. No loss of consciousness. There is no fecal or urinary incontinence. Following the attack the patient feels exhausted for one to two hours.

The attacks have been experienced for the past eight years and with increasing frequency until at present there is almost one attack a day. The patient states that for a period of 1 to 2 minutes she can "feel them coming on." There is no special cause assigned to them but a "start" has often initiated them. The patient feels they are more common 1 to 1½ hours after meals.

Past personal and family histories are irrelevant.

Physical examination reveals a well-developed and nourished white female. Objective findings are negative. Pulse, 110; respiration, 20; blood pressure, 146/98; blood and urinalysis, negative; Wassermann and Kahn, negative; electrocardiogram, sinus arrhythmia; roentgenograms of chest, negative. The heart is not enlarged.

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Cholecystogram, negative. Gastric analysis (Ewald), free acid 35, total acid, 45; complete blood chemistry, normal; sugar tolerance test, normal; basal metabolic rate = 0.

Of several attacks that occurred during period of observation in the hospital, blood pressure readings were obtained almost throughout in two instances and rose to a maximum of 270/140 and 236/136 respectively several minutes after onset. Blood sugars obtained at these periods were 84 mg. per cent and 157 mg. per cent respectively.

Intravenous pyelograms: negative on both sides, questionable mass upper pole of left kidney.

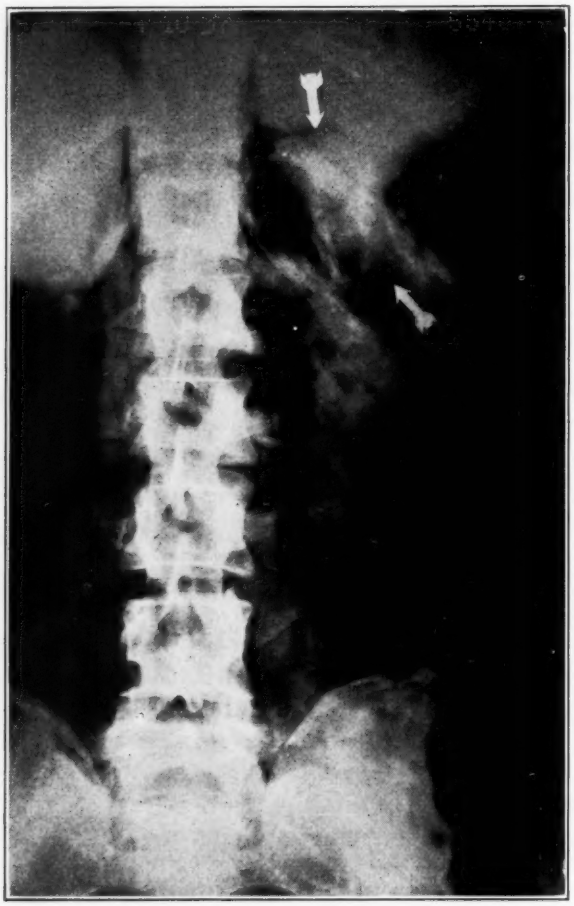

Fig. 1.—Roentgenogram after left perirenal injection of air. Arrows indicate spheroidal tumor mass at upper pole of left kidney.

Retroperitoneal injections of air about the left kidney were performed by one of us (N.R.) and roentgenograms then revealed a rounded soft tissue mass at the upper pole of the left kidney.

Clinical diagnosis: Left suprarenal tumor (pheochromocytoma) producing paroxysmal hypertension.

Exploratory laparotomy, April 21, 1937. Novocain spinal anesthesia, later ethylene. The abdomen was entered through a high midline incision. Exploration of the lower abdomen was negative. A rounded, firm, moveable mass was palpated

in the region of the left suprarenal gland. The right and left kidneys felt normal. The right suprarenal gland was palpated and found to be normal. No other abnormalities were present. The stomach was drawn and held downward pulling the lesser omentum taut. A longitudinal slit was then made in the midportion of the latter and the right index finger introduced backward through the posterior parietal peritoneum until the upper border of the body of the pancreas was felt. The tumor mass was then grasped by the left hand through intact right portion of lesser omentum and immobilized against the exploring right index, middle, and fourth fingers which had also been introduced through the enlarged rent in the lesser omentum and posterior parietal peritoneum. Palpation about the tumor with the fingers of the right hand revealed a definite encapsulation and by digital dissection the mass was separated easily from surrounding areolar tissue. This digital dissection was carried out with great care since large vessels going into the tumor were anticipated; furthermore it was hoped to identify a principal vascular pedicle and clamp it before its vessels might have been opened. However, such a pedicle was not encountered. The tumor to all practical purposes appeared floating in the retroperitoneal areolar tissue. It shelled out readily and was removed through the route of access. One moderate sized vessel was clamped and tied. Since no bleeding ensued following removal of the tumor, re-exploration of the site was limited but no left adrenal was identified. During the digital dissection, the upper pole of the left kidney was constantly palpated. The opening in the lesser omentum was closed and the abdominal wound closed in layers.

Blood pressure readings were made at 5-minute intervals during the operation which lasted 1 hour and 30 minutes and are summarized as follows:

Preoperative	120/80
After spinal anesthesia	90/60
Tumor manipulated in freeing it	220/140 (for 30 min.)
5 min. after removal of tumor	160/100
10 min. after removal of tumor	125/90
15 min. after removal of tumor	90/60
15 to 25 min. after removal of tumor	No pressure reading obtainable
500 c.c. normal saline venoclysis begun; 35 minutes to 70 minutes after the tumor was removed the pressure varied between	90/80 and 120/90

The postoperative course was uneventful and no "attacks" were experienced. Frequent blood pressure readings varied from 98/76 to 134/90.

The patient has been seen at intervals during a period of one year following operation. No "attacks" have occurred and the patient states she feels completely relieved of her former symptoms except for occasional tachycardia. The blood pressure has become stabilized at approximately 135/80.

PATHOLOGIC STUDY

Gross Description.—The tumor is a rounded, well-encapsulated mass measuring 7 by 5.5 by 5 cm. and weighing 75 gm. It is soft and in places feels cystic. When bisected the fresh surfaces are yellowish red to gray and there are several cystic spaces containing yellowish fluid or what appears to be clotted blood. The largest cystic space measures 1.5 cm. in diameter and is near the center. One portion of tissue bordering this space is definitely yellow over an area 3 by 1.5 cm. It is definitely firmer than the remainder of the mass.

Microscopic Study.—Sections from various regions of the tumor show a marked degree of vascularity as evidenced by the large numbers of sinusoid-like blood spaces separating cords of tumor cells. The latter vary in appearance in different regions.

In places they appear as huge processed syncitium-like masses with giant nuclei. In other regions the cells strongly resemble those of the normal suprarenal medulla and elsewhere those of the adrenal cortex, with typical vacuolated cytoplasm. In some fields the cells appear to have been markedly compressed into fusiform shape by surrounding blood-filled sinusoids. In general the nuclei are rounded or oval with finely divided chromatin and one nucleolus. The cytoplasm is eosinophilic and finely granular. The appearance after chromate fixation is striking. Almost all of the tumor cells—even the vacuolated ones—show either diffuse browning of their cytoplasm or brown granulations. There is considerable extravascular browning of stroma and of the precipitate in blood vessels. A few coarse brownish hyaline granules (not seen in formalin-fixed sections) are present both in and outside tumor cells.

A section through the thick hyaline capsule shows a narrow rim of what appears to be atrophic adrenal cortex, outside the capsule. While these cells are not unlike some of the tumor cells, there is absolutely no chromaffinity, although the tumor

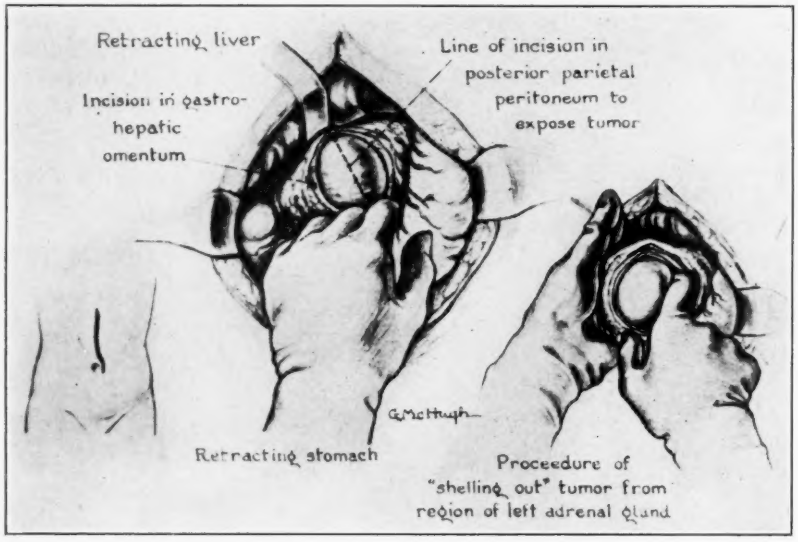
Retracting liver
Line of incision in posterior parietal peritoneum to expose tumor
Incision in gastro-hepatic omentum
G. McHugh
Retracting stomach
Procedure of "shelling out" tumor from region of left adrenal gland

Fig. 2.—Semidiagrammatic illustration of excision of left suprarenal pheochromocytoma through gastrohepatic omentum.

cells on the inside of the capsule are deeply browned. One section shows a recent fibrin thrombus in a large blood space and scattered foci of necrosis in the tumor.

Pathologic diagnosis: Pheochromocytoma, left adrenal gland.

Operative Procedures.—Eleven previous instances of pheochromocytoma have been reported to date in which operative removal was successful and was followed by relief of the "attacks." These cases are summarized in Table I. Case 9 is recorded as pheochromocytoma because of the positive histologic findings (positive chromate reaction), but from the clinical history there were no paroxysmal attacks of hypertension. This patient presented a persistent "hypertension" of 190 to 160 systolic pressure. Of 10 cases (that of von der Muhl not included) 6 were removed through a lumbar or kidney incision and 4 through abdominal incisions. In our opinion it would appear that the abdominal incision has advantages over the lumbar incision even though accurate

localization of the tumor is possible by pneumoretroperitoneography for the following reasons: (1) Multiple tumors may be present and the lumbar incision would not permit thorough exploration of the retroperitoneal spaces. (2) There may be congenital absence of one adrenal

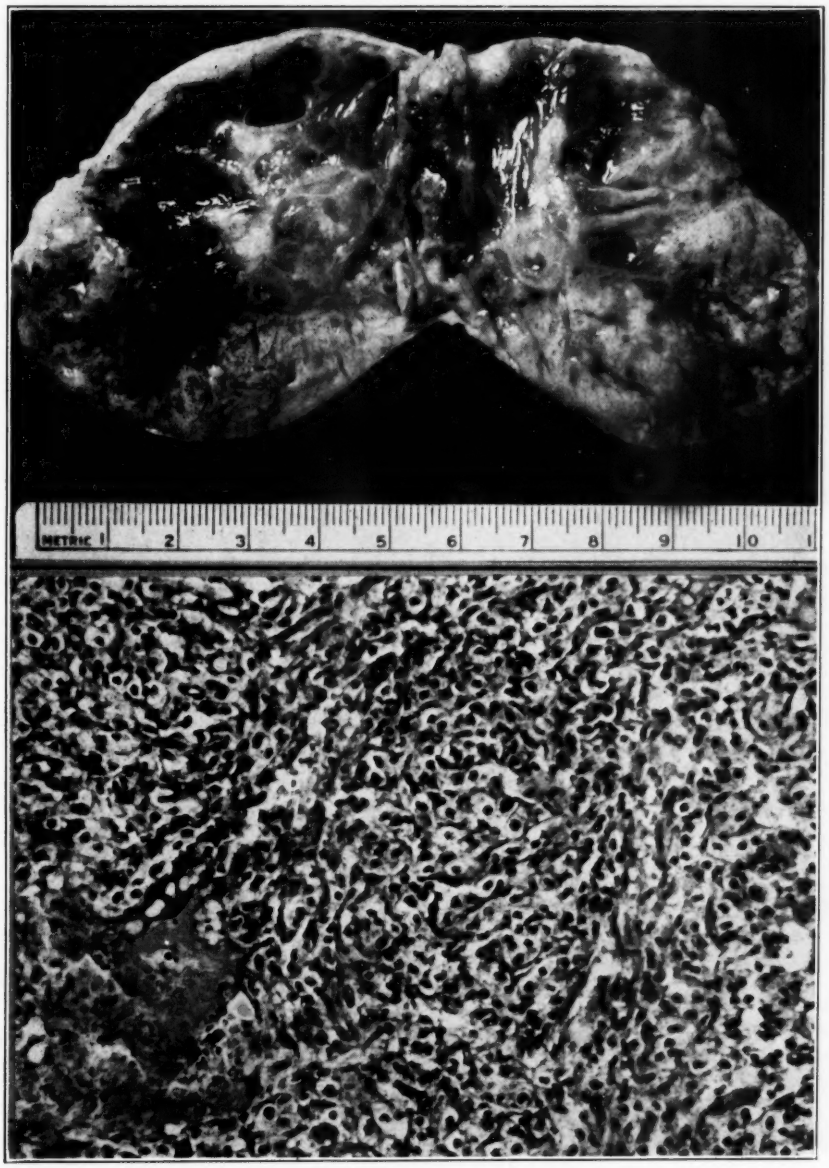

Fig. 3.—Gross and microscopic appearances of excised pheochromocytoma.

gland. (3) Where, as in some reported instances, the tumor is on the anterior aspect of the kidney and adherent to surrounding tissues, sparing this kidney would be more feasible from an anterior approach than through a lumbar incision.

TABLE I

SUMMARY OF SUCCESSFUL EXCISIONS OF PHEOCHROMOCYTOMAS REPORTED UP TO 1937

CASE	AUTHOR	PROCEDURE	BLOOD PRESSURE DURING OPERATION	POSTOPERATIVE COURSE
1.	Mayo, C. H. (1927)	Female, aged 30 years: upper midline incision to removal of tumor 6 by 4 cm. behind tail of pancreas on mesial side of left kidney	Not reported	Relief from ''attacks''; convalescence uneventful except pulmonary infarction which developed two weeks after operation and lasted for 10 days; recovery
2.	Shipley, A. M. (1929)	Female, aged 26 years: first operation high left rectus incision, tumor palpated anterior to upper pole of right kidney and was not removed; second operation, incision coursing below right costal arch to removal of tumor mass 8 cm. in diameter	Variation from 130 to 140 systolic; no ''attacks'' during operation; fall to 88/62 after tumor was removed	Relieved of symptoms; last report 10 months after operation
3.	Porter, M. F., and Porter, M. F., Jr. (1930)	Male, aged 39 years: midline incision converted into T-shaped incision for removal of mass on anterior aspect of right kidney	Systolic pressure 110 at beginning, rose to 264, and dropped to 78 toward end of operation when adrenalin was given	Well for 74 days; no further note
4.	Suermondt, W. F. (1934)	Male, aged 29 years: ''fist-sized'' tumor removed from upper pole of right kidney through loin incision	Fall of blood pressure during operation to a ''very low level'' (75-60 systolic); no other readings recorded	Recovery from operation and free from attacks during six months following it
5.	Coller, F. A., Field, H., and Durant, T. M. (1934)	Male, aged 16 years: small midline incision to permit palpation with finger; incision then enlarged to removal of mass 8 cm. in diameter from anterior aspect of right kidney	Blood pressure 150/120 at beginning and rose to 300/140 after one hour; shortly after removal of tumor, fell to where no reading could be obtained; after recovery from operation, 130/90	Followed for 6 months; no recurrence of attacks

TABLE I—CONT'D

6.	Kalk, H. (1934)	Female, aged 36 years: right loin incision to removal of fist sized tumor at upper pole of right kidney, "adrenal vessels" going to it	Normal blood pressure readings during and following operation	Recovery from operation although complicated by right-sided pneumonia and parotitis
7.	Leriche, R. (1934)	Male, aged 41 years: right suprarenal region previously explored; left kidney incision to removal of cherry-sized tumor from retroperitoneal fat above left kidney	Before anesthesia 220/135; during excision of tumor, 240/150; during closure of wound, 160/100; during convalescence, 140/100	Uneventful; no recurrence of attacks
8.	Von der Muhl (1934)	Reference not available; quoted by Belt and Powel.		
9.	McKenna, C. M., and Hines, L. E. (1935)	White female, aged 59 years: right lumbar incision to removal of right kidney with tumor 12 by 9 cm. connected to upper pole and densely adherent to surrounding structures; no typical attacks of paroxysmal hypertension reported; blood pressure was 190 to 160 systolic	Not reported	Convalescence prolonged due to "hypochromic anemia" and persistent suppurative fistulous tract; blood pressure 98/48
10.	Kelly, H., Piper, M., Wilder, R., and Walters, W. (1936)	Female, aged 37 years: right posterolateral (kidney) incision for removal of tumor mass 10.5 cm. in diameter invading suprarenal gland	"At the onset of the operation the blood pressure was normal and there was little variation during the time of operation"	Uneventful; blood pressure remained normal
11.	Beer, E., King, F. H., and Prinzmetal, M. (1937)	Female, aged 26 years: left lumbar incision to removal of spheroidal tumor 9 cm. in diameter occupying region of left adrenal gland, pushing kidney downward	No rise in blood pressure during operation but at one time systolic pressure fell to 80 cm.	Postoperative course uneventful; blood pressure 125/85

The Blood Pressure During Operation.—In 9 cases of the above series, including the one reported here, blood pressures were observed at frequent intervals during the removal of the growth. In 4 no rise was noted at any time during the operation; in 4 there was a rise to well above 200 systolic (as observed during attacks preoperatively) when the tumor was manipulated and removed and then rapidly fell to a level at which readings could not be obtained for a short period when a return to approximately 70 to 90 was then recorded (therapeutic measures to combat shock were of course instituted). In Leriche's case the pressure had risen to an "attack level" after induction of anesthesia but fell to an unmeasurable level when the small tumor was removed.

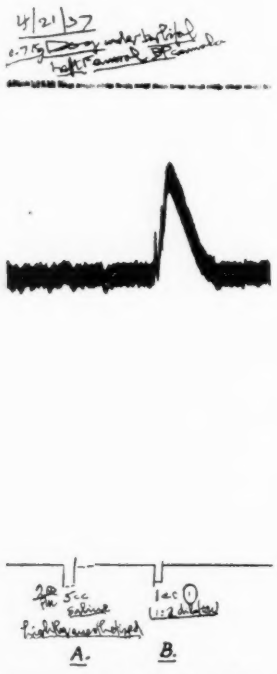

Fig. 4.—Tracing of blood pressure of 10.7 kg. dog under barbital anesthesia. *A*, injection of 5 c.c. saline solution intravenously; no perceptible effect on blood pressure. *B*, injection of 1 c.c. dilute HCl extract of pheochromocytoma; rapid rise in blood pressure for brief period, a "typical adrenalin curve" (experiment performed by Dr. Louis Leiter).

Analysis of the Tumors for Adrenalin.—The origin of these neoplasms from chromaffin tissue has led to a study of their adrenalin content. Table II summarizes the more recent observations.

In normal adrenal glands there is approximately 1 to 2 mg. of adrenalin per gram of tissue. In the above series such values were obtained for some tumors while very high values, such as 20 to 40 mg., were obtained in others. Various factors might account for small variations in the results of analyses, such as inclusion in the assayed tissue of portions of normal adrenal medulla and cortex. On the other hand, the

TABLE II

SUMMARY OF ANALYSES OF PHEOCHROMOCYTOMAS FOR ADRENALIN

AUTHOR	SPECIMEN	CHEMICAL METHOD OF ANALYSIS	ADRENALIN CONTENT OF TUMOR
Rabin (1929)	Tumor from autopsy 40 gm.	Folin (colorimetric)	1.5 mg. per gm.
Belt and Powel (1934)	Tumor from autopsy 1,000 gm.	Folin	20 mg. per gm.
Kalk (1934)	Tumor and kidney tissue surgical specimen	Zanfrognini	30 to 40 mg. per gm.
Burgess, A. M. (1936)	Tumor from operation (died postoperatively)	Folin	3.5 mg. per gm.
Kelly, et al. (1936)	Tumor from operation 240 gm.	Folin	1 mg. per gm.
Popken, C. (1936)	Tumor from autopsy 6 by 5 by 4 cm.	Pharmacologic method? Effect on blood pressure of decerebrated cat	9 mg. per gm.
Fein and Carman (1937)	Tumor from autopsy; weight not stated	Not stated	22 mg. per gm.
Edwards (1937)	Tumor from autopsy 20.7 gm.	Folin	3.94 mg. per gm.
Humphreys (1937)	Tumor from autopsy 35 gm.	Folin	2.5 to 3 mg. per gm.*
(Unpublished case from University of Chicago Clinics)			
Brunschwig, Humphreys, and Roome (1938)	Tumor removed at operation, 75 gm.	Folin	1.25 mg. per gm.*

*Adrenalin determinations were made by Dr. J. M. Rogoff, of the Department of Physiology.

very high values, if true, would indicate a marked hyperactivity on the part of the neoplastic cells in the production of adrenalin.

There is no apparent explanation for the paroxysmal character of the attacks of hypertension. That such attacks are due to sudden outpouring of an excess of adrenalin is inferred from the excess of adrenalin producing tissue represented by the tumor and by the relief from such attacks following removal of these tumors. Final confirmation of this is afforded by the observation of Beer, King, and Prinzmetal, who demonstrated a pressor substance (adrenalin) in the blood of a patient during an attack.

A possible explanation for the paroxysmal nature of the attacks is that the secretion of adrenalin by the tumor is controlled to some extent by the same mechanism which controls the secretion from the normal

adrenal glands and that when such a mechanism calls for a sudden release of adrenalin into the circulation the tumor tissue also responds.

SUMMARY

A review is made of the eleven cases of paroxysmal hypertension due to retroperitoneal pheochromocytoma in which successful operative removal resulted in relief from symptoms. An additional case is recorded.

Experience has shown that such tumors are eventually fatal, even though not malignant, because of the repeated hypertensive attacks with ultimately a very severe one with fatal collapse. Sufficient experience has been gained to permit the recognition of these tumors by the characteristic clinical syndrome and such a diagnosis should indicate operative removal of the tumor. The repeated successes of the latter modify the previous pessimistic prognosis held for such cases.

REFERENCES

Belt, A. E., and Powel, T. O.: Surg. Gynec. & Obst. **59**: 9, 1934.
Beer, E., King, F. H., and Prinzmetal, M.: Ann. Surg. **106**: 85, 1937.
Burgess, A. M., Waterman, G. W., and Cutts, F. P.: Arch. Int. Med. **58**: 433, 1936.
Coller, F. A., Field, H., and Durant, T. M.: Arch. Surg. **28**: 1136, 1934.
Edwards, D. G.: J. Path. & Bact. **45**: 391, 1937.
Fein, M., and Carman, F. F.: Am. J. Cancer **29**: 301, 1937.
Kalk, H.: Klin. Wchnschr. **13**: 613, 1934.
Kelly, H., Piper, M., Wilder, R., and Walters, W.: Proc. Staff Meet. Mayo Clin. **11**: 65, 1936.
Leriche, R.: Lyon Chir. **31**: 355, 1934.
Mayo, C. H.: J. A. M. A. **89**: 1047, 1927.
McKenna, C. M., and Hines, L. E.: J. Urol. **31**: 93, 1935.
Popken, C.: Beitr. z. Path. Anat. **97**: 337, 1936.
Porter, M. F., and Porter, M. F., Jr.: Surg. Gynec. & Obst. **50**: 160, 1930.
Rabin, C. B.: Arch. Path. **7**: 288, 1929.
Shipley, A. M.: Ann. Surg. **90**: 742, 1929.
Suermondt, W. F.: Zentralbl. f. Chir. **61**: 70, 1934.
Vaquez, H., Donzelot, E., and Gerandel, E.: Presse méd. **37**: 169, 1926.
Von der Muhl: Cited by Belt and Powel.

TWO CASES OF MALIGNANT PERINEAL TUMOR SIMULATING INFLAMMATORY LESIONS

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CARCINOMA of the perineum, with the exception of epidermal neoplasms, is exceedingly rare, and, because of its rarity, we believe a report of two cases is indicated. During the past two years we have had the opportunity of studying two highly malignant primary perineal tumors which simulated inflammatory lesions. We have been unable to discover any description of a similar growth by personal inquiry or by a fairly exhaustive review of recent and past literature. Less than a dozen cases of malignant perineal tumors have been reported in adults and these consist of squamous cell carcinoma, sarcoma, and adenocarcinoma. A survey of the standard textbooks of pathology and surgery has afforded scanty, if any, pertinent information concerning these peculiar lesions. In general, all types of malignant tumors of the perineum are remarkable for their infrequency; however, it is conceivable that their frequency is greater than the statistics would indicate. The two cases reported here are the only cases of this nature in 113,922 admissions at the University Hospitals of Cleveland in the period from 1923 to 1937.

At the time the patients were first examined, the outstanding features of both cases were pain, the evidences of inflammation, and the short duration of the lesions. We wish to emphasize their symptomatology, clinical course, similarity, and type. These tumors must be differentiated from acute or subacute inflammatory, granulomatous, or benign neoplastic lesions.

CASE REPORTS

CASE 1.—The first patient, a 16-year-old Italian girl, came to the Out-Patient Department in August, 1934, complaining of a painful swelling on the right side of the anal region of one month's duration. Examination revealed a dumbbell-shaped, nonfluctuant, moderately tender, firm mass extending transversely across the perineum anterior to the anus (Fig. 1). The overlying skin was slightly reddened and edematous. The right side was slightly the larger. No abnormal lymphadenopathies were found at this time. No ulceration or involvement of the vaginal or rectal mucosa had occurred.

This lesion was thought to be of a low grade inflammatory nature, and ambulatory treatment consisting of hot sitz baths was advised. In spite of this therapy the mass progressively enlarged and failed to soften. Tests with Frei antigens were inconclusive. One month later, biopsy of the perineal mass submitted for

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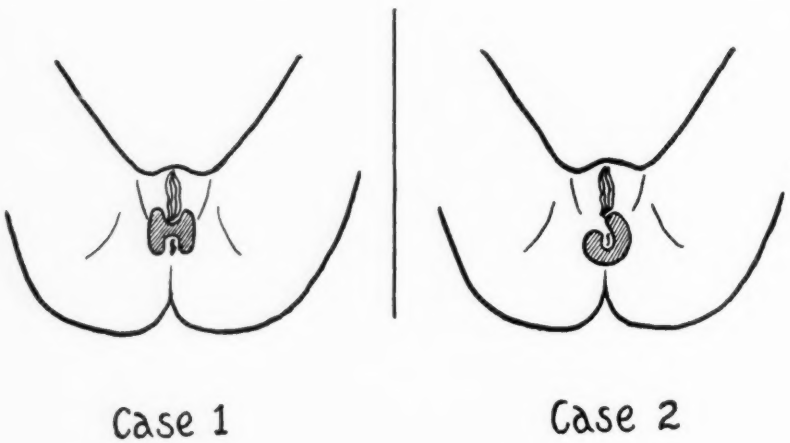

Fig. 1.—Diagrams showing area of involvement.

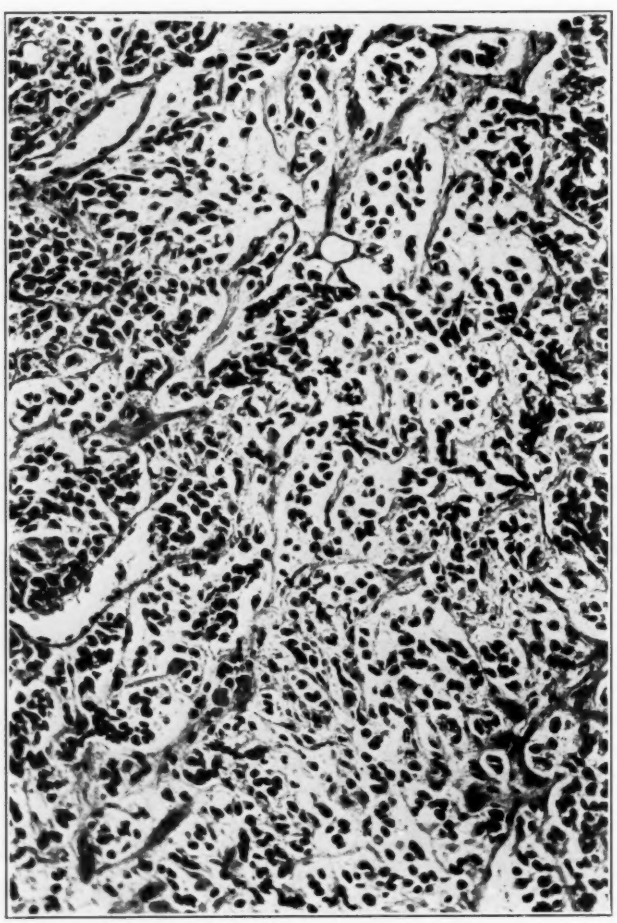

Fig. 2.—Photomicrograph of Case 1. The tumor is composed of small cells which have large hyperchromatic nuclei. It shows indistinct lobulation.

microscopic examination showed small cell carcinoma (Fig. 2) and an excised inguinal node revealed metastasis. Roentgen ray therapy was instituted and the primary tumor disappeared. The patient became progressively worse and widespread metastases occurred (Fig. 3). She died nine months after the onset of symptoms. No autopsy could be obtained.

CASE 2.—The second patient was an 18-year-old colored girl who entered the hospital in October, 1936, complaining of a painful swelling near the rectum of one month's duration (Fig. 1). At its onset it appeared on the left side, was moderately tender, and gradually progressed around behind the anus to the right side. Bowel movements had been painful. Her father had died three years previously of pulmonary tuberculosis.

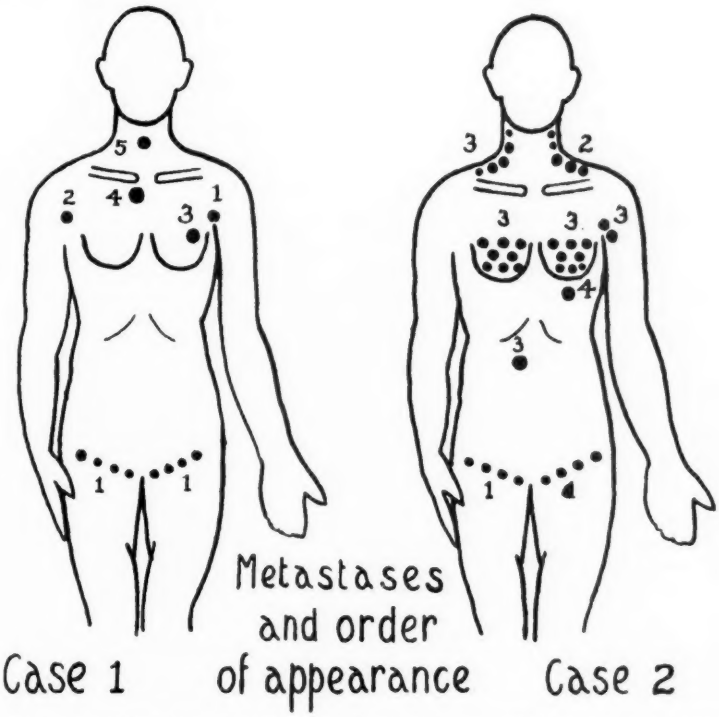

Fig. 3.—Diagrammatic representation of massive gross metastases as observed before death.

The salient features of the examination were: The temperature was normal. The white blood cell count was 10,000. The perineum was warm, tense, indurated, swollen, and edematous. This indurated area encircled the anus posteriorly in the shape of a horseshoe. The rectovaginal septum was free of induration. No ulceration of the rectal mucosa was found. Small firm inguinal nodes were palpable. Roentgenograms of the spine and chest were normal. Investigation of the genitourinary and gastrointestinal tracts revealed them to be normal. For all purposes this lesion appeared to be inflammatory; however, one of us had had the opportunity of seeing the first patient, and, with that case in mind, a tentative diagnosis of neoplasm was made in this instance. It was thought best that the mass should be incised and if no pus was obtained a biopsy should be procured. No pus was obtained and some tissue was removed for microscopic study. This revealed it to be a small cell carcinoma (Fig. 4). An excised inguinal node showed the same type of tumor.

Radiation therapy was immediately begun by Dr. Eugene Freedman, and the perineal tumor and enlarged inguinal nodes entirely disappeared. Five months later the first apparent metastases were noted, these being in the left supraclavicular space. This was the beginning of a rapid dissemination of the tumor, and metastases were soon apparent in both sides of the neck, both breasts, left axilla, mediastinum, and the skin of the back of the neck and abdominal wall (Fig. 3). The patient had continuous epigastric pain, and bilateral hydrothorax and ascites developed. Respirations became increasingly difficult because of tracheal compression and the increasing pleural fluid. She gradually became comatose and died in

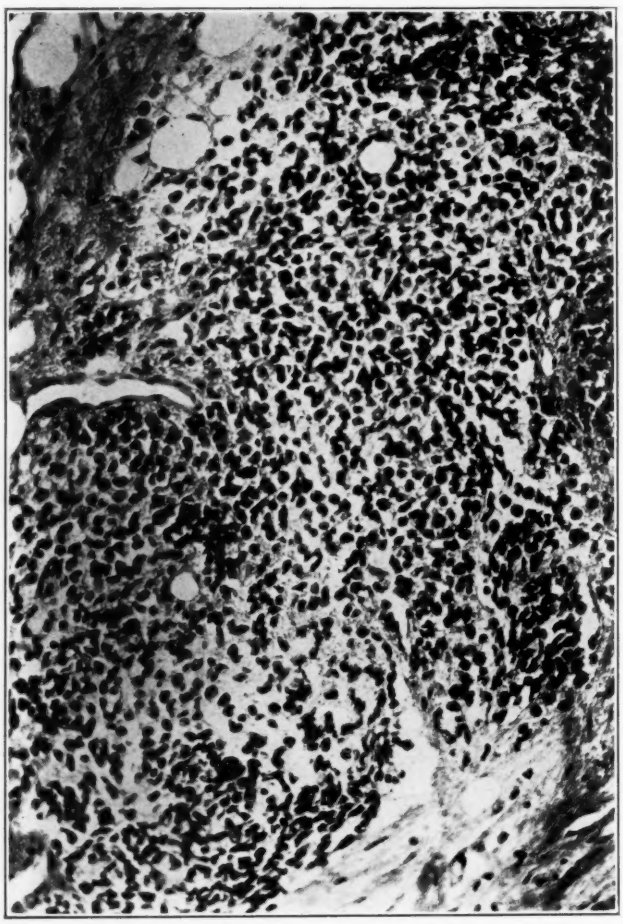

Fig. 4.—Case 2. The tumor is composed of small cells having a scanty amount of cytoplasm and very large pleomorphic nuclei. The tumor in Case 1 presented some areas suggestive of alveolar differentiation.

the sixth month of her illness. Shortly before her death the blood urea nitrogen was 110 mg. per cent and creatinine, 10.8 mg. per cent.

Autopsy was performed by Dr. William Wartman. The external genitals were normal. The anus presented an entirely normal gross appearance, while only rarely were bizarre cells found in the interstices of fibrotic and atrophic muscular tissues in the surrounding regions. The most striking finding was the presence of tumor tissue which had involved in a massive fashion all the perivertebral lymph nodes from the pelvis to the base of the skull. A huge retroperitoneal mass was found

surrounding the ureters and extending into the spleen. The esophagus and trachea were encircled by similar masses. No normal lymphatic tissue was recognizable. A small nodule could be demonstrated in the right ventricle. An interesting finding was the fact that no tumor could be demonstrated in either the lungs or liver.

The similarity of these two interesting cases is at once apparent. Both were in the anal region; both simulated inflammatory lesions; both had widespread metastases; and both were of short duration.

Little is known concerning the cytogenesis of these tumors. The most tenable theory is that they arose from embryologic tissues which were misplaced during the development of the perineum. Most malignant tumors of this region—and they too are uncommon—are mucus-secreting tumors and undoubtedly have their origin embryologically in the remnant of the hind gut. In the past three months we have seen two cases of epidermal carcinoma of this region which did not involve the rectum.

The objective characteristics of inflammation can be explained on a basis of lymphedema resulting from lymphatic blockage, as is often seen in cancer of the breast.

We report these cases with the hope that recognition of other cases will lead to a better understanding of the lesion. We can only assume that the original lesions for which the patients presented themselves represent the primary lesions and this seems justifiable.

REFERENCES

Aschenborn, O.: Sarcoma perinei, Arch. f. klin. Chir. **25**: 174, 1880.

Burtenshaw, J. H.: Epithelioma of Perineum, Tr. Path. Soc. Phila. **16**: 226, 1891-3.

Castex, M. R., and Llambías, C. A.: Metastases in Hip Bone Originating in Epithelioma Developed in an Aberrant Perineal Node, Rev. Soc. de med. int. y Soc. de tisiol. **6**: 373, 1930.

Eberhard, T. P., and Warren, S.: Mucous Gland Tumors of Female Perineum, Am. J. Cancer **23**: 334, 1935.

Goecke, H.: A Case of Cancer of the Perineum, Zentralbl. f. Gynäk. **57**: 117, 1933.

Gross, S. W.: Fibrocystic Tumor; Multiple Cystic Tumor or Cystomatous Sarcoma of the Perineum, Phot. Rev. M. & S. Phila. **1**: 13, 1870-71.

Hellendall, H.: Ein Adenokarzinom des Dammes, Zentralbl. f. Gynäk. **49**: 477, 1925.

Heyfelder, O.: Exstirpation eines Faserkrebses aus der Nähe des Afters, Deutsche Klin. **2**: 440, 1850.

Jung, Jakob: Ueber einen Fall von Carcinom der Damm- und After-gegend, Freiburg, 1897, G. Melhase.

Kough: Schirrus of Perineum with Cancerous Infiltration of Subperitoneal Glands, Lancet **2**: 975, 1880.

Leischner, H.: Large Myxosarcome of Perineum, Beitr. z. klin. Chir. **148**: 226, 1929.

Schwartz, E.: Sarcome globo-cellulaire de la région périnéale à marche inflammatoire; ablation avec résection du bulbe de l'urèthre, Ann. de mal d'org. génito-urin. **10**: 114, 1892.

Syme, J.: Cancer of Perineum; Excision; Recovery, Edinburgh M. & S. J. **44**: 13, 1835.

CONGENITAL ANORCHIA, WITH A REPORT OF SIX PROBABLE CASES OF MONORCHIA

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CONGENITAL absence of one or both testicles in man is rare. The medical records of the War Department for the World War report only 52 cases of anorchia in the first two million men examined. Undoubtedly many of these cases and many reports in the literature are confused with arrested migration of the testicle, castration, fusion of the two testes, transverse ectopy, etc.

Cabrol in 1564 reported the first case of congenital bilateral anorchia. From then until 1878, when Gruber reviewed the literature, only 29 verified cases of anorchia had been recorded; of these 7 were bilateral and 22 unilateral; Gruber observed a case of monorchia, which made a total of 23 cases.

Counseller and Walker could find only 9 instances of bilateral anorchia in the available literature up to 1933, and added 2 cases of their own. In 1936 Fleet examined 1 case of unilateral absence of the testis and found that 5 additional cases had been reported since Gruber's series.

Thus, to date, only about 40 cases of anorchia have been recorded; of these 11 were bilateral and 29 unilateral.

St. Hilaire believes that in many cases where absence of one or both testicles has been reported, these organs exist hidden in the abdomen or are atrophic. He doubts if many cases are authentic and states that all reports should give exact details about the arrangement of the other parts of the seminal apparatus. However, embryologically, there is a possibility that a testis like any other organ may be absent, and similar anomalies have been found in the opposite sex and in lower animals. Marchand reports the absence of a left ovary and the greater portion of the tube and broad ligament in a girl, 1 year old. Hobday has found cases of a bilateral anorchid colt and a monorchid horse and states that it is an "occasional" occurrence in animals.

At best, the evidence to prove a case of anorchia is circumstantial, but if after careful anatomic and histologic examination one fails to find a testis, one may conclude that the gonad was congenitally absent, barring operative interference. Detailed and careful search at necropsy should be sufficient to determine the presence or absence of gonads. Such thorough search in persons who are operated upon, of course, is not possible.

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During the last eight years at the University of Minnesota Hospitals, 6 cases of probable monorchia have been observed. All the cases were operated upon by O. H. Wangensteen, whose interest and general acquaintance with the subject of the undescended testis are well known. The preoperative diagnosis in these cases was cryptorchidism, but at exploration no testis was found. It is possible that the testis lay hidden elsewhere in the body and was not accessible at operation, but, apart from a gonad in a remotely aberrant position, the absence of the testis is likely. Because of the rarity of this condition at operation and its possible relationship to other anomalies, the following cases are reported:

CASE REPORTS

CASE 1.—L. H., hospital number 54368, aged 8 years, was admitted to the University of Minnesota Hospitals June 4, 1930, and discharged June 17, 1930. He was admitted with the diagnosis of bilateral undescended testis since birth. He also had a slight convergent strabismus.

Physical examination was essentially negative. The left testicle could not be palpated, but the right testicle could be felt in the inguinal canal. It was freely movable, but could not be brought into the scrotum. Examination of the blood and urine was essentially negative.

On June 5, 1930, the patient was operated upon. On the left side, after opening the external oblique aponeurosis, the gubernaculum was seen to come down posterior to the parietal peritoneum and to imbed itself deep to the Poupart ligament. There was no definite evidence of testis. A small hernial sac was felt. This was dissected free from the gubernaculum and ligated. A small band was found to run behind the bladder in the usual course of the vas deferens. This could not be identified as vas. No internal spermatic artery was found. Exploration of the retroperitoneal space and peritoneal cavity with the finger revealed no testis. Immediately overlying the left femoral artery was a small hard mass which appeared to be a lymph node. This and the gubernaculum and anociated structures were removed. Microscopic sections of the tissues removed (Hospital operation 30-954-5-6-7-8) showed several lymph nodes, gubernaculum, and vas deferens. A hernioplasty was performed on both sides and an orchiopexy on the right.

CASE 2.—W. O., hospital number 642893, aged 16 years, was admitted to the University of Minnesota Hospitals Oct. 15, 1935, and discharged Nov. 11, 1935. Since birth he had had undescended testes. He had never noticed the testes in the scrotum or felt them in the canals. His home doctor had injected the left inguinal canal for hernia.

Physical examination revealed the penis and scrotum to be somewhat underdeveloped. The testicles were not felt in the scrotum or in the inguinal region. The patient had a congenital heart lesion, probably on the basis of pulmonary stenosis. His general appearance was that of a cretin. A prostatic smear was negative for spermatozoa. Basal metabolic rate was +6 per cent.

On Oct. 18, 1935, the patient was explored through a right oblique inguinal incision. No testis was found. Dissection was made far into the retroperitoneal region as far as the bifurcation of the aorta. The peritoneal cavity was opened also, but no trace of testis, vas deferens, or gubernaculum was found. A hernioplasty was performed and the wound closed. On Nov. 1, 1935, an orchiopexy was performed on the left side.

CASE 3.—A. B., hospital number 639502, aged 24 years, was admitted June 13, 1935, and discharged June 26, 1935. The patient said the left testicle had never been felt. The right testicle had always been normal in size and position. No hernia could be demonstrated on physical examination nor could the left testicle be palpated.

On June 14, 1935, through a left inguinal incision, the patient was explored. There was a spermatic cord in which the vas deferens and vessels were found. No testis was found. The retroperitoneal space was explored. Failing to find testicular tissue, the vas deferens was amputated near the bladder and the spermatic cord cut high in the retroperitoneal region. A small hernial sac was found which was ligated. A Bassini hernioplasty was done in the usual fashion.

CASE 4.—G. S., hospital number 55234, aged 8 years, was admitted Aug. 12, 1930, and discharged Aug. 23, 1930. For two years prior to the admission, it had been noted that the left testis of the patient was not in the scrotum. At no time had it caused him any discomfort.

Physical examination was essentially negative except that no left testicle could be felt. The right testis was normal in size, shape, and position. The external genitals were normal.

On Aug. 13, 1930, an operation was performed. On dividing the external oblique aponeurosis, the terminal end of the spermatic cord was seen to insert into the outer leaf of the external oblique aponeurosis. It did not extend into the scrotum. With the slightest traction, it was detached. Upon following this medially the vas and spermatic vessels were seen, both of which were extremely small. What seemed to be testis and epididymis were mere nubbins of tissue, about ⅕ or ⅙ the size of the other testis. This tissue was removed, but on cut section proved to be scar tissue. No testis was found. An indirect inguinal hernia was repaired.

Microscopic study of the removed tissue (Hospital operation 30-1399) showed no evidence of testicular tissue. There were epididymis, spermatic cord, spermatic blood vessels, muscle and fibrous connective tissue (gubernaculum?) present.

CASE 5.—R. U., hospital number 640161, aged 11 years, was admitted July 24, 1935, and discharged Aug. 7, 1935. The patient had a right inguinal hernia and bilateral undescended testis. One year before he had had a right herniorrhaphy elsewhere, at which time no right testis was found.

On July 25, 1935, the patient was operated upon and a recurrent right indirect inguinal hernia was repaired. A normal spermatic cord was found, but no definite testis was isolated. In the retroperitoneal space there was a small piece of tissue that was thought to be testis as there was a small vascular pedicle running from it toward the renal region. This tissue and the spermatic cord in the inguinal region were removed for histologic study. A hernioplasty according to Andrews' technique was performed.

Microscopic sections of the removed tissue (Hospital operation 35-2080 and 2079) showed fibrous tissue, blood vessels, and a small lymph node.

CASE 6.—W. R., hospital number 664234, aged 20 years, was admitted March 16, 1938, and discharged March 28, 1938.

The patient had presented bilateral undescended testis since birth. A year before his home doctor had tried anterior pituitary-like substance (antuitrin-S) with no results.

The right testis could be felt overlying the external oblique aponeurosis, having migrated out to the external abdominal ring. There was an indirect inguinal hernia present. A testis could not be felt nor a hernia on the left side.

A right orchiopexy and hernioplasty was performed Dec. 3, 1937.

The patient returned March 17, 1938, at which time the scrotal-crural anastomosis on the right was undone and exploration carried out through a left oblique inguinal incision. The conjoined tendon was intimately attached to the external oblique aponeurosis at Poupart's ligament. There apparently was no vas deferens. A tiny remnant of a structure coming from the bladder on the outside of the peritoneum may have represented vas deferens. The gubernaculum extended into the scrotum. There was no testis or spermatic vessels that could be found.

A hernioplasty was performed.

Microscopic sections of the tissues removed (Hospital operation 38-802-3-5-6) revealed probable vas deferens, fibrous tissue, and blood vessels; no testis.

DISCUSSION

1. *Etiology.*—Congenital absence of the testis is said to be due to prenatal atrophy resulting from intrauterine disease or trauma, or to partial or total failure of embryonic development of the sex glands. Counseller and Walker, however, do not believe that any disease process, either before or after birth, could occur which would not leave some remnant of tissue that could be identified. Furthermore, the association of this anomaly with absence of the kidney and ureter, extrophy of the bladder, imperforate anus, urethrorectal and vesicorectal fistulas (Collins, Boyden, Walker and Guinard) strengthens the belief that anorchia is a developmental defect.

2. *Varieties of Anorchia.*—This anomaly may exist in various degrees. Sebileau and Descomps claim that there is no report in the literature of complete absence of the deferent canal, but Velpeau and Blandin have reported complete unilateral absence of the testicle and seminiferous pathways (Thorek). Gruber reported 5 instances where the testis, epididymis, and part of the vas deferens were missing and 5 other cases where the testis was absent but the epididymis and ductus deferens present. A summary of his findings in our cases is tabulated in Table I.

It is interesting that unilateral anorchia is more common on the left side. The incidence of left- to right-sided absence of the testis is 2:1 according to Sebileau and Descomps and 4:1 according to Godard. In our series the deformity was four times on the left and twice on the right.

3. *Relation of Anorchia to*

A. *Development of the Secondary Sex Characters:* A bilateral anorchid is a true natural eunuch with feminine aspect and development (Thorek). On the other hand, the external genitals and secondary sex characters of a monorchid may develop normally. It may be difficult to distinguish among a monorchid in which the one testis is abdominally retained, a cryptorchid with abdominal gonads, and a bilateral anorchid. In fact, up to puberty it is impossible to differentiate these entities.

TABLE I

SUMMARY OF THE FINDINGS IN SIX PROBABLE CASES OF MONORCHIA

NAME	NUMBER	AGE	DIAGNOSIS	MONORCHIA							
				SIDE	TESTIS	EPIDIDYMIS	VAS DEFERENS	SPERMATIC VESSELS	PROSTATE	HERNIA AT OPERATION	GUBERNACULUM
G. S.	55234	8 yr.	Left undescended testis	Left	Absent	+	+	+		+	+
L. H.	54368	8 yr.	Bilateral undescended testes	Left	Absent		+	+		+	+
W. O.	642893	16 yr.	Bilateral cryptorchidism; congenital heart disease (pulmonary stenosis); left inguinal hernia	Right	Absent	Absent	Absent	Absent	Normal	+	Absent
R. U.	640161	11 yr.	Bilateral undescended testes; inguinal hernia	Right	Absent	Absent	+	+		+	
A. B.	639502	24 yr.	Left undescended testis	Left	Absent	Absent	+	+	Normal	+	
W. R.	664234	20 yr.	Bilateral undescended testes; inguinal hernia	Left	Absent	Absent	?	?	Normal	+	+

After puberty, it still may be impossible to distinguish between a cryptorchid with abdominal gonads and a monorchid with an abdominal testis. Both may develop normal secondary sex characters. However, distinction may be made between these conditions and complete anorchia, not only by the lack of secondary sex characters in the latter, but also by the status of the genital function (Godard). A man congenitally deprived of both testes is impotent; he is able to have rare erections, but he does not ejaculate semen. He differs from the double cryptorchid or monorchid in that such patients, if they have one functioning testis, are potent and may be able to reproduce.

Of the three cases past puberty in this series, two were normal as to secondary sex characters. The third patient (W. O.), aged 16 years, had the appearance of a cretin; the penis and scrotum were underdeveloped.

B. *Hernia:* As mentioned above, it is impossible to differentiate by inspection alone between the congenital absence of testes and cryptorchidism; in fact, most anorchids are thought to be cryptorchids before operation. Some authors have stressed the presence or absence of hernia in the differential diagnosis of these two conditions. It is known that all cryptorchids have a potential, if not an actual, hernia. Eccles found that more than one-half of the cases of retained testes actually have an associated hernia. Counseller and Walker found in their series that, when definitely stated, a hernia was not present in 5 anorchids. They believe that if a hernia is absent and the testes not palpable, while the testes are probably only undescended, they may be completely absent.

While this may be a valuable sign, it should be emphasized that 3 of 6 of our cases had an associated inguinal hernia which was diagnosed before operation, and at operation all 6 cases had evidence of a hernia. Similarly Dass and Berry have reported the absence of the testes with hernia. Thus, while absence of a hernia and failure to palpate the testes may suggest anorchia, it should be remembered that anorchia may be present with a coexisting hernia.

C. *Pseudohermaphroditism:* If the patient has a perineal hypospadias, undescended testes, and anomalies of the secondary sex characters, the possibility of pseudohermaphroditism should be considered. While hermaphroditism and pseudohermaphroditism are rare, they are more common than anorchia, and the similarity of the anomalies may obscure the true diagnosis. Urethroscopy may be of diagnostic value in these cases, for what was thought to be a normal urethra may actually be a persistent urogenital sinus into which a hypoplastic vagina opens. One of the cases (W. R.) was examined with an urethroscope by C. D. Creevy after operation to rule out this possibility; no other anomaly was found.

D. *Cryptorchidism:* At the University of Minnesota Hospitals, 143 cases of undescended testes have been seen. To date, 6 cases of probable monorchia have been operated upon (4.2 per cent). Whether there is some relationship between anorchia and cryptorchidism is speculative.

It is generally known that there are degrees of separation of the epididymis from the testes in cryptorchidism. Counseller and Walker suggest that cases of anorchia may represent a final degree of separation with resulting atrophy and disappearance of the testis.

Hunter believed the undescended testis to be congenitally imperfect. If this be true, one would expect to find a gradation in cryptorchidism from absence of the testis to almost perfection. Other writers, such as Moore and Wangensteen, while accepting that some retained testes are imperfect *ab initio*, believe that most of the imperfection becomes manifest at puberty as the result of temperature, hormonal and pressure influence. Certainly it is impossible to distinguish grossly or microscopically between a descended and undescended testis up to puberty. Moreover, most of the ectopic testes seen shortly after puberty show the upper degrees of development and only with time do atrophic changes appear.

For these reasons, it is believed that the incidence of anorchia to cryptorchidism in this series (4.2 per cent) is probably coincidental and not of significance. The final word as to a possible relationship cannot be said, however, until the cause of these two conditions is known.

SUMMARY

Congenital anorchia is a rare anomaly. To date about 29 unilateral and 11 bilateral cases have been reported in the available literature.

Six cases of probable monorchia are presented in this paper. Four of these occurred on the left side and 2 on the right. Three cases had an associated inguinal hernia, which was diagnosed before operation, and at operation all 6 cases had evidence of hernia. The possible relationship of anorchia to other anomalies, such as cryptorchidism, hermaphroditism, etc., has been discussed.

REFERENCES

1. War Department Record: Defects Found in Drafted Men. Statistical Information Compiled from the Draft Record, Washington, 1920, pp. 72, 164.
2. Gruber: Quoted by Fleet.
3. Cabrol: Quoted by Gruber.
4. Counseller, V. S., and Walker, M. A.: Congenital Absence of Testes, Ann. Surg. **98:** 104, 1933.
5. Fleet, R. H.: Congenital Anorchia, Brit. J. Urol. **8:** 141, 1936.
6. Saint Hilaire: Des Anomalies de l'Organization **1:** 502.
7. Marchand: Berl. klin. Wchnschr. **15:** 813, 1894.
8. Hobday, F.: Cryptorchidism in Animals and Man, Proc. Roy. Soc. Med. **17:** 3, 1923.
9. Collins, D. C.: Congenital Unilateral Renal Agenesia, Ann. Surg. **95:** 715, 1932.

10. Boyden, E. A.: Congenital Absence of the Kidney, Anat. Record **52:** 325, 1932.
11. Walker, T. J.: Genito-urinary Surgery, New York, 1914, Funk & Wagnalls Company, p. 756.
12. Guinard, L.: Precis de Teratologic Anomalies et Monstrosities Chez L'Homme et Chez les Animaux, Paris, 1893, p. 252.
13. Sebileau and Descomps: Quoted by Thorek, M., and Thorek, P.
14. Thorek, M., and Thorek, P.: Anorchidism (Absence of the Testicle), J. Urol. **30:** 345, 1933.
15. Godard, E.: Note sur l'absence congenitale du testicule, Compt. rend. Soc. de biol. **11:** 311, 1859.
16. Dass, H.: Inguinal Hernia in a Monorchid, Brit. M. J. **2:** 717, 1929.
17. Berry, J. J.: Two Cases of Absence of One Testicle with Hernia, New England M. Monthly **1:** 197, 1881.
18. Creevy, C. D.: Pseudohermaphroditism. A Report of Five Cases, Internat. S. Dig. **16:** 195, 1933.
19. Wangensteen, O. H.: The Undescended Testis: an Experimental and Clinical Study, Arch. Surg. **14:** 663, 1927.
20. Moore, C. R.: Biology of the Testis, Baltimore, 1934, Williams & Wilkins Company, Chap. VII. Sex and Internal Secretion.
21. Hunter, J.: Works of John Hunter (Palmer), Animal Economy **4:** 1839.
22. Eccles, W. M.: Abstract of the Hunterian Lectures on the Anatomy, Physiology and Pathology of the Imperfectly Descended Testis, Brit. M. J. **1:** 503, 1902.

TORSION OF THE UTERINE ADNEXA

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TORSION of the uterine adnexa must be classed among the rarer gynecologic crises. Although a number of observers have described the clinical symptoms and operative findings, the standard textbooks allot the condition scant mention, with the result that, comparatively unknown to the majority, it goes unrecognized and an accurate preoperative diagnosis is seldom made. The surgeon confronted with a twisted gangrenous tube is often unable to discuss his case intelligently until he has consulted his library.

While torsion of the pedicle of ovarian cysts is relatively common, torsion of the Fallopian tubes, with or without torsion of the ovaries, is encountered more rarely. In the three cases which the writer is reporting, Case 1 showed bilateral tubal torsion, both ovaries being normal; in Case 2 there was torsion of the right tube only, the other adnexa revealing no pathology; and in Case 3 both the right tube and the right ovary were involved in the torsion, while the left tube was adherent from the isthmus to the fimbriae to a large multilocular cyst of the left ovary.

The etiology of torsion of the adnexa has never been adequately explained. Anspach believes the exciting causes of torsion of the tube are the same as those producing torsion of the pedicle of ovarian cysts and quotes Storer: "disturbance of the equilibrium of the tumor by irregular growth, changes in abdominal pressure during pregnancy, and immediately following labor, distention and evacuation of the bladder, difference in pressure during the act of emptying the bladder, peristalsis, sudden movements of the body, and trauma, including gynecological examinations." Other writers, attempting to prove that torsion can occur in perfectly normal adnexa, list trauma and peristalsis as the most plausible causative factors, and in support of their theory call attention to the more frequent occurrence of right-sided torsion. They reason that the muscles of the right side of the body are used more often than those of the left for heavy lifting, etc., and that the anatomic arrangement of the organs on the right side gives more leeway for peristalsis to produce torsion than is possible on the left where the sigmoid wedges the contents of the left pelvis in place. Shute believes the foundation is laid in fetal life when the tube is considerably longer than the overlying peritoneum and therefore assumes convolutions and spirals, and that this discrepancy persists to about puberty and is common even in adults. In explanation of adnexal torsion both

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Shute and Anspach refer to the studies of Payr and Sellheim. Briefly stated the theory is as follows: The artery or arteries in the pedicle of an organ are shorter, thicker, and obviously less distensible than the veins in which the circulation is tortuous. Payr found that by injecting under uniform pressure the pedicle of a spleen resting on water (injecting the artery and veins simultaneously), he was able to produce rotation of the organ in an arc of 125 degrees. Although the writer has not encountered this particular deduction, Payr's theory might explain not only the rare phenomenon of torsion of the omentum, but also volvulus and intussusception. The circulatory disturbance combined with peristalsis might act as the causative factor.

In order to gauge the possibility of torsion in the normal adnexa, it might be well to review their anatomy. The normal tube is approximately 12 cm. in length. There are four subdivisions: the short uterine portion, the slender isthmus, the ampulla, which is the dilated outer two-thirds, and the fimbriated funnel-shaped infundibulum. The muscular wall grows progressively thinner from the isthmus outward. There are three coats: the serous, underlying which are found the blood vessels and nerves; the muscular, the outer layer of which is longitudinal and the inner layer circular; and the mucosa. Although the outer two-thirds of the tube appear much thicker, this is simply due to the arborescent corrugations of the mucosa. The outer two-thirds of the tube are obviously heavier and tend to fall downward and inward on the posterior surface of the broad ligament. Frequently, one of the fimbriae is attached to the outer pole of the ovary. The writer has made gentle efforts to produce torsion in the normal tube by grasping the ampulla with forceps and twisting it both clockwise and counterclockwise. The tube is returned promptly to its former position. The ovaries are held in place by the meso-ovarium, a double layer of peritoneum springing from the posterior surface of the broad ligament. Between the laminae run the blood vessels and nerves to enter the hilum of the gland. There are, besides two other supporting structures, first, the ovarian ligament, consisting of smooth muscle, lying between the layers of the broad ligament and extending from the uterine extremity of the ovary to the lateral aspect of the uterus where it is attached between the origin of the tube and the origin of the broad ligament; second, the ligament commonly known as the infundibulopelvic ligament, which extends from the tubal or outer extremity of the ovary to the lateral wall of the pelvis and is the lateral fifth of the broad ligament unoccupied by the tube. It is attached, after crossing the external iliac vessels, to the fascia and peritoneum covering the psoas major muscle. This ligament carries the ovarian vessels and nerves.

It is a moot question whether the normal tube is ever the site of torsion. In the three cases observed by the writer, the increase in weight of the distal portion of the tube was due either to a collection of fluid,

or in one case to the presence of an ovarian cyst with elongated ligaments, and the enormously thickened and congested meso-ovarium was highly suggestive of the vascular origin of the torsion. There was nothing in the appearance of the tubes suggestive of either a congenital deficiency of the peritoneal coat or of the presence of the fetal spiral type except, of course, the twists. As Anspach remarks: "The normal Fallopian tube is of such size and structure that strangulation by torsion is almost inconceivable. When, however, the outer part of the tube becomes enlarged or heavy, and is not adherent to the surrounding parts, the mechanical conditions favoring torsion may be said to exist, viz., a freely movable tumor (the enlarged ampulla of the tube), attached to a more or less fixed base (the uterus) by a pedicle (the isthmus of the tube and the mesosalpinx). Under such circumstances the same forces which cause torsion of ovarian or parovarian tumors may come into play with a similar result." On the other hand, Shute holds that inflammation is a debatable etiologic factor; that a pliable normal tube should twist more easily than a thickened inflamed one. It is impossible to arrive at a definite conclusion, and the solution is just about as deducible as whether the egg or the chicken came first in the scheme of existence. Even histologic examination of an operative specimen offers no proof for the changes in the tube tend to obscure the picture for the pathologist. When a gangrenous tube is sent to the laboratory, it is very difficult to distinguish whether it was diseased before the torsion took place, or if the pathology has been produced by the torsion. In the cases reported of pyosalpinx and hydrosalpinx with closure of the ostia, the causative pathology is more apparent. Hematosalpinx, however, might be the result and not the cause of torsion.

Torsion of the adnexa is probably a more common occurrence than the rarity of its recognition would indicate. It is possible for the adnexa to become twisted and to right themselves without intervention. In a number of instances there is even distinct evidence that self-amputation of the tube has taken place with subsequent absorption. In one case, autopsy on an aged woman disclosed the calcified remains of what appeared to be an ovary adherent to the pelvic wall. So far the writer has been unable to find any record of a fatal case. The abdominal cavity may just as well be able to care for a self-amputated tube as it does for the placenta after cesarean section for abdominal pregnancy. It follows, therefore, that nature might deal adequately with the majority of these cases without operative interference. Certainly, our surgical training inclines us to remove at once any gangrenous intra-abdominal organ. In the past there must have been many cases where spontaneous recovery resulted. But since torsion has occurred in tuberculous or otherwise infected tubes, and we cannot be certain of the pathology until laparotomy is performed, expectant treatment is strongly disapproved. On two occasions I have made a pre-

operative diagnosis of torsion of the tubes only to find at operation cystic ovaries adherent to the posterior surface of the broad ligament, which were causing intermittent attacks of agonizing pelvic pain. In several other instances I believe slight torsions occurred which righted themselves after rest in bed or at the termination of pregnancy.

The symptoms of adnexal torsion are easily confused with those of appendicitis, and this may be one explanation for the greater number of right-sided torsions found at operation. There is a tendency toward conservative treatment in left-sided abdominal pain. The symptoms also may be ascribed to ectopic pregnancy. The attacks of pain are sudden in onset and intermittent at intervals of days, months, or years. Constipation, nausea, and vomiting usually are concomitant. There is, as a rule, a rise in temperature and leucocytosis. While many writers believe that a history of trauma can be elicited, others cite examples of the pain coming on in the middle of the night's slumber or during a prolonged hospital stay in bed. There is also the same difference of opinion as to relation to the menses. The following characteristics were common to the three cases observed by the writer:

1. Sudden onset of abdominal pain, paroxysmal and severe, which soon became localized laterally in the pelvis.

2. Nausea and vomiting from twelve to twenty-four hours after initial symptoms.

3. Absence of constipation.

4. No apparent relation to menses, since one case occurred two weeks after the last period; one, nine days; and the third, six months after menstruation had ceased.

5. None gave a history of trauma or of unusual exertion.

6. Examination in each case showed a tender mass of indefinite outline and doughy consistency, lateral to the uterus.

7. All gave histories of prior attacks of pain, similar in location but of less intensity.

On the other hand, two showed leucocytosis (18,000 and 20,000) with a neutrophile count of 88 per cent and 92 per cent. The third had a count of 8,000 with 68 per cent neutrophiles. Temperatures upon admission to the hospital were respectively 101°, 101.5°, and 97.5°; pulse rates, 118, 100, and 60. Two developed dark, bloody, foul discharge some hours after the onset of pain, while one had no discharge whatever. In all three cases the affected tubes were found gangrenous at operation.

CASE REPORTS

CASE 1.—Mrs. C., aged 32 years, two induced abortions, no full-term children. Last abortion occurred three years before she was seen by me and was followed by a few days of fever which did not rise above 100°. One year after this, she complained of acute pain in the right ovarian region. The appendix had been removed

several years previously. She was seen by a physician who told her that the ovary and tube had become twisted and that she would probably be all right with a few days' rest in bed. On the second day the pain abated, and on the third day she was able to resume her usual activities. A year later she had a similar attack, but called no physician, the pain subsiding after four or five hours. When seen by me, she was in a condition of mild shock. The lower abdomen was rigid; temperature was 100°. There was a slight dark bloody discharge. The menstrual period had occurred two weeks before. Blood count, 18,000 leucocytes, with 88 per cent neutrophiles. Vaginal examination showed intense tenderness and a doughy mass on each side of the uterus. She was taken to the hospital at once. The abdomen was opened in midline and both tubes found twisted one and one-half times and purplish black. The right tube was twisted in a clockwise direction; the left tube counterclockwise. The distal thirds of both tubes were distended with clear fluid. A bilateral salpingectomy was performed. No adhesions were noted in the region of the cecum. There was no serum or blood in the peritoneal cavity. The ovaries were normal and were not disturbed. This attack occurred on the fourteenth day after the first day of menstruation.

Case 2.—Mrs. G., aged 26 years, para i, normal pregnancy three years before. No history of fever during the puerperium. No history of menstrual disturbance. Patient was brought to Mercy Hospital, New Orleans, suffering with intense pain on the right side. The appendix had been removed five years prior to admission. She related that she had had two attacks of lesser intensity but with pain of the same character; the first, six months before admission; and the second, one year before. Blood count, 20,000 white cells, with a differential of 92 per cent neutrophiles.

The abdomen was opened in midline. The right tube was twisted clockwise two and one-half times and was bluish black in color. It was removed. The right ovary and left adnexa were normal. There were no adhesions at the site of the appendectomy. Examination of the tube showed the ostium closed and the ampulla distended with clear fluid. Recovery of patient was uneventful.

Case 3.—Mrs. M., aged 42 years, normal weight 167 pounds, present weight 117 pounds; two children, aged 22 and 19 years. Periods started at eleven years, were regular, and lasted from eight to ten days. Both deliveries were normal. One induced abortion after four months' gestation eleven years ago; short, but febrile, convalescence. Tertian malaria ten years ago. Six years ago she began to have pain in the right chest, followed by five days of fever ranging from 99° to 101°. This pain was thought to be pleurisy; a year later pain developed over the right hip. Examination revealed a small right ovarian tumor. The periods since then have been three to four months apart and very profuse, lasting from ten to twelve days. For three years she has had almost daily pain lasting from five to thirty minutes. The last period occurred six months before admission to the hospital. She believed she was changing life prematurely. Three months ago she had paroxysmal pelvic pain that lasted several days.

Examination in 1932 showed an anteflexed uterus containing numerous small fibroids. On the right side of the abdomen there was a mass which was thought to be a small ovarian cyst. The left side was practically normal. She was advised at the time, on account of the frequency of the pain, to have an operation. I was of the opinion that the pedicle of the cyst had become twisted from time to time. I next saw her professionally in September, 1935. She had been feeling ill for five days but had been confined to bed for twenty-four hours only. The attack was ushered in by paroxysmal pains in the right lower quadrant. After twenty-four

hours, a dark, bloody discharge appeared which she believed to be a menstrual flow. On the third day of the attack, she had nausea and vomiting. The pain gradually became worse, the paroxysms lasting from fifteen to twenty minutes, but being comparatively infrequent, as, at times, two or three hours were spent in comfort. The temperature was 97.5°; pulse, 60; total white count, 8,000; neutrophiles, 67 per cent; blood pressure, 126 systolic and 80 diastolic. General examination, aside from the usual picture of undernutrition, was essentially negative. There was no distention of the abdomen and no rigidity. There was no tenderness at McBurney's point. Pressure over Poupart's ligament on the right side produced pain. Vaginal examination showed an anteflexed uterus studded with fibroids. On the left side a tense mass, occupying the entire space between the uterus and the wall of the pelvis, was felt. On the right side a soft doughy mass, exquisitely tender, could be palpated next to the uterus. Slightly lateral to it, the ovarian cyst, discovered at the previous

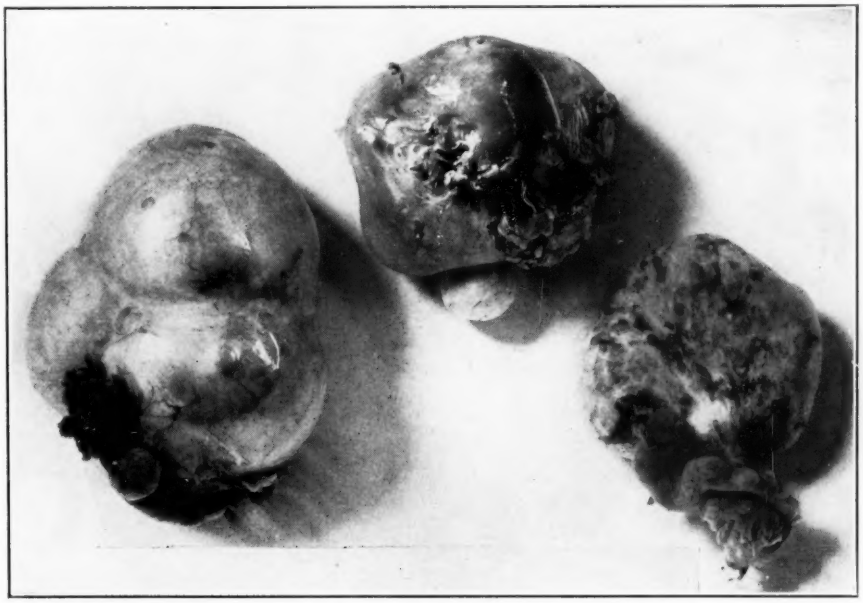

Fig. 1.—The left ovary shows a multilocular cyst, no torsion. The right ovary shows the mottling described in the pathologic report. Tortuous tube and elongated and thickened ovarian ligament.

examination, could be made out. I was struck by the absence of any signs of shock. She was sent to the hospital for observation and operation was performed the next morning.

Operation.—Midline incision was extended from the symphysis upward to a point just below the umbilicus, sweeping to the left of the umbilicus and carried down to the rectus sheath, about one inch above it. The rectus sheath was divided and the left and right recti retracted. The peritoneum was opened in the midline. Inspection of the pelvis showed a uterus studded with fibroids. Immediately behind the left broad ligament was a large multilocular ovarian cyst (Fig. 1) with the left tube adherent from the isthmus to the fimbriae. Tube and cyst were removed en masse. The right adnexae were not at first visible. Palpation of the cul-de-sac showed the right ovary and right tube gangrenous as a result of torsion. The tube showed four clockwise twists and was completely devitalized to the cornu. It was clamped at its junction with the uterus, and tube and ovary were removed en masse.

A supravaginal hysterectomy was then done. No free fluid was found in the pelvic cavity. The appendix was grossly normal; it was removed. The stumps of the infundibulopelvic and round ligaments were sutured to the cervix. The abdominal wall was closed in layers without drainage.

Laboratory report.—The specimen received consisted of uterus, right and left tubes, with large cystic ovaries attached, and an appendix.

The uterus is irregular in shape, having several nodular growths, varying in size, located within its wall; it measures 6 by 6 by 7 cm. The outer surface is partially covered by smooth, glistening peritoneum with a few lacerations over the fundus, evidently due to the application of instruments at time of operation. The remainder of the surface is rough and irregular showing fibrous tags and several blood vessels. On the posterior surface near the isthmus there is found a subserous leiomyoma, measuring 2 cm. in diameter. The color of the uterus is normal pink. Palpation reveals a varying consistency and several nodules located in the muscular coat which are firm, while the remainder of the musculature is more or less flabby. Incision through the uterus shows the wall to vary in width from 1¼ cm. at the isthmus to

Fig. 2.—Another view of both ovaries. The white area at the attachment of the ovarian ligament to the ovary was entirely bloodless.

2½ cm. at the fundus. The lumen is outlined by smooth, glistening endometrium which measures about 2 mm. in thickness. Its surface shows small petechial clots near the fundus and covering the leiomyoma lying in this region. There are several leiomyomas in the wall of the uterus that vary in diameter from 1 cm. to 2½ cm. and which are located throughout the wall of the uterus, some being submucosal and others subserous.

The left ovary (Fig. 2) is made up of three large cystic cavities. The largest of the two measures 3 cm. in diameter; the smaller one, 2½ cm. in diameter. Scattered over the surface are a few small cysts which vary from ½ to 1 cm. in diameter. The outer surface is covered by smooth, glistening peritoneum, bright pink to gray in color. Palpation reveals a fluctuant consistency. An incision through the ovary shows it to be made up completely of cystic cavities, there being no normal ovarian tissue remaining. The contents of the cysts are fluid of a straw color. The lining of the cysts is smooth, glistening, and shows no irregularities.

The salpinx attached to the ovary measures 9 cm. in length and varies in width from 4 mm. at the fimbriated end to 6 mm. at the ampulla. The fimbriated end is found patent. The outer surface is smooth, glistening, and pink in color. At-

tached to the tube in the region of the ampulla is found a thin-walled cyst, containing clear straw-colored fluid, and measuring 1 cm. in diameter.

The right ovary (Fig. 2) measures 6½ to 7 cm. in width, 7 cm. in length and 3 cm. in thickness. Its outer surface is covered by smooth, glistening membrane which is mottled in color, there being the deep red, purplish color of a hemorrhagic cyst, the small light pink striations of congested blood vessels, patches of extravasated blood into the tissues of the ovary. The light gray to yellow color is that of the follicular cysts. The ovary is found attached to the tube by a pedicle which measures 3 cm. in length and 4 cm. in width. It is covered by smooth, glistening peritoneum and shows quite a bit of congestion of its tissues.

The tube attached measures 12 cm. in length and varies in width from 3 mm. at the isthmus to 6 mm. at the ampulla. The fimbriated end is found patent and is of a light pink color. The remainder of the tube is gangrenous. The broad ligament measures 3 cm. in width, ½ cm. in thickness.

The appendix measures 5 cm. in length and ½ cm. in width. Its outer surface is covered by a smooth, glistening membrane, light pink in color. The blood vessels show some slight degree of congestion. Palpation reveals a firm consistency, the appendix having the feel of a fibrous cord. Incision through the appendix shows the lumen to be patent, containing a small amount of mucus and feces. The mucosa is smooth and glistening, light pink in color, with an occasional hemorrhagic spot.

Microscopic Diagnosis.—Hyperplasia of the endometrium, slight fibrosis of the wall of the uterus, multiple leiomyomas of the wall of the uterus, multiple follicular cysts of the right and left ovaries, with congestion of the blood vessels and extravasation of blood into the tissues surrounding the blood vessels and cysts; left salpinx normal except for moderate congestion. The blood vessels and supporting tissues of the right ovary show congestion. Chronic inflammatory appendicitis.

REFERENCES

Anspach, Brooke M.: The Torsion of Tubal Enlargements with Especial Reference to Pyosalpinx, Am. J. Obst. **66**: 553, 1912.

Darner, H. L.: Torsion of the Normal Fallopian Tube, Am. J. Obst. & Gynec. **11**: 368, 1926.

Downer, I. G., and Brines, O. A.: Torsion of Undiseased Uterine Adnexa in Virgins, Am. J. Obst. & Gynec. **21**: 665, 1931.

McEachern, A.: Torsion of the Normal Fallopian Tube, Brit. M. J. **1**: 190, 1934.

Papikoff, N.: On the Axial Rotation of Cysts of Fallopian Tube Tumors, J. Obst. & Gynaec. Brit. Emp. **43**: 286, 1936.

Payr, Erwin: Weitere experimentelle und klinische Beitrage zur Frage der Stieldrehung intraperitonealer Organe und Geschwülste, Deutsche Ztschr. f. Chir. **85**: 392, 1906.

Shute, Evan: Comments on Torsion of the Adnexa with a Report of Illustrative Cases, Am. J. Surg. **16**: 490, 1932.

THE CAUSE OF DEATH IN BILE PERITONITIS

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ALTHOUGH bile peritonitis is relatively uncommon, the mortality rate is excessively high, usually given around 50 per cent; it has been shown that it accounts for a significant number of deaths following operations upon the biliary tract. As soon as the importance of this hitherto rarely recognized condition was demonstrated, numerous experimental attempts were made to ascertain the mechanism of death in bile peritonitis.

It is quite obvious that infected bile inundating the peritoneal cavity might engender a suppurative or pyogenic peritonitis, the same as perforation of an infected appendix; the malignant character of this type of bile peritonitis is conceded by most authors, consequently the efforts of most investigators have been applied to determine the effects of sterile bile in the peritoneal cavity.

The opinions are controversial and may be placed into two categories:

A. Sterile bile in the peritoneal cavity is innocuous. Noetzel,[15] McWilliams,[13] Orth,[16] Sich and Fraenkel,[21] Buchanan,[3] Ritter,[19] Fraenkel and Krause,[5] and many others.

B. Sterile bile in contact with the peritoneal surfaces is harmful. In the latter group there are again divided opinions which may be classified as follows: (1) Death in choleperitoneum is due to the toxicity of one or more components of bile, especially the bile salts. Wangensteen,[23] Horrall,[10, 11] Horrall and Carlson,[12] Brand,[2] Rywosch.[20] (2) Death is due to endogenous infection; that is, the bacterial factor, especially *Clostridium welchii*. Rewbridge and Hrdina,[17, 18] Andrews, Rewbridge, and Hrdina,[1] Dvorak.[4] (3) Shock from fluid loss is the chief lethal factor. Harkins, Harmon, Hudson, and Andrews,[7-9] Trusler and Martin,[22] Moon and Morgan.[14]

In order to demonstrate the noxiousness of intraperitoneal sterile bile and, more specifically, to determine the cause of death in choleperitoneum, several series of animals were subjected to procedures designed to imitate as closely as possible the circumstances under which the condition occurs clinically. This, of course, is only crudely accomplished and only by inference can the theories thus obtained from such experiments be applied to patients.

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THE TOXICITY OF BILE SALTS

In order to determine the relative toxicity of the sodium taurocholate and sodium glycocholate, we injected intramuscularly varying quantities of the commercial salts in sterile solution into guinea pigs weighing between 498 and 512 gm.

TABLE I

GUINEA PIG	WEIGHT IN GM.	SODIUM TAUROCHOLATE MG.	SODIUM GLYCHOLATE MG.	REMARKS
19	510	200		Living and well, 8 days
20	500	300		Killed, 4 days
21	506	500		Died, 3-4 days
22	498	700		Died, 1 day
23	511	500		Died, 3 days
24	508	500		Died, 3 days
25	510		500	Died, 4 days
26	512		500	Died, 3 days
19*	508		300	Living and well

*Used for second time eight days after first experiment.

It is thus seen that the toxicity of the bile salts is roughly quantitative in its action, and that in this series there was little difference to be seen in the relative toxicity of the two bile salts used.

Throughout this experimental work, lethal doses of bile were calculated on the basis of its bile salt content; this was determined by the method of Gregory and Pascoe[6] which is based upon the color produced by the interaction of bile salts with furfural in a sulfuric acid solution, heated. This color is compared in a colorimeter with a standard concentration of bile salt solution similarly and simultaneously treated. The color is due to the cholic acid portion of the conjugated bile acids. We found the cattle bile, which was mainly used in our experiments, to contain from 95 to 170 mg. of bile salts per cubic centimeter; dog bile, about 200 to 250 mg. per cubic centimeter; human gallbladder bile, about 46 mg. per cubic centimeter.

THE BACTERIAL FACTOR

Into nine dogs, cattle bile or human bile was injected intraperitoneally.

In the four dogs that died, the peritoneal fluid was cultured in brain broth, and in every case gas was present in the culture and large gram-positive rods with truncated ends were present either in pure or in mixed culture.

In two dogs pure cultures of *Clostridium welchii* were injected into the peritoneal cavity with no untoward results: (1) Dog 12 A, 18.2 kg., 30 c.c. Welch culture injected intraperitoneally; well six weeks; (2) Dog 17, 6.8 kg., 10 c.c. Welch culture injected intraperitoneally; well six weeks.

TABLE II

DOG	INJECTION, INTRAPERITONEAL	DEAD OR WELL	WEIGHT IN KG.	AMOUNT PERITONEAL FLUID	CULTURE OF PERITONEAL FLUID
1 A	91 c.c. human bile; sterile; 4,100 mg. bile salts	Well	13.0		
2 A	150 c.c. human bile; sterile; 6,900 mg. bile salts	Well	15.0		
3 A	500 c.c. human bile; sterile; 23,000 mg. bile salts	Well	17.0		
4 A	200 c.c. human bile; sterile; 9,200 mg. bile salts	Dead 24 hr.	11.3	175 c.c.	Pure culture, gm. + rods, no gas
5 A	100 c.c. cattle bile; sterile; 105 mg. bile salt per c.c.	Dead 12 hr.	7.3	90 c.c.	Mixed culture, gas
6 A	100 c.c. cattle bile; sterile; 105 mg. bile salts per c.c.	Dead 24 hr.	18.2	90 c.c.	Pure culture, gm. + rods, gas
7 A	100 c.c. cattle bile; sterile; 105 mg. bile salts per c.c.	Dead 24 hr.	9.1	95 c.c.	Mixed culture, gas
10 A	100 c.c. human bile; 46 mg. bile salts per c.c.	Well	13.0		
11 A	100 c.c. human bile; 46 mg. bile salts per c.c.	Well	15.0		

In three dogs the fundus of the gall bladder was amputated without tying the common bile duct; in three others the gall bladder was defundated, and the ductus choledochus was ligated and divided. These operations were performed under aseptic technique. In all six dogs, the bile, the liver, and the abdominal muscle were cultured for a gram-positive anaerobe simulating *Clostridium welchii*. The dogs died in from two to twelve days and varying amounts of hemorrhagic and bile-

TABLE III

DOG	PROCEDURE	BILE CULTURE	MUSCLE CULTURE	LIVER CULTURE	DEATH	PERITONEAL FLUID	CULTURE PERITONEAL FLUID
1 B	Gall bladder defundated	+	-	-	2 days	300 c.c.	+
2 B	Gall bladder defundated	+	+	+	12 days	150 c.c.	+
3 B	Gall bladder defundated	-	+	+	7 days	500 c.c.	-
4 B	Common bile duct tied and cut Gall bladder defundated	-	+	-	9 days		+
5 B	Common bile duct tied and cut Gall bladder defundated	-	+	+	2 days	300 c.c.	+
6 B	Common bile duct tied and cut Gall bladder defundated	-	+	+	2 days	250-300 c.c.	+

stained ascitic fluid were found. This fluid was cultured in each case. A gram-positive large rod similar to *Clostridium welchii* was found in five cases.

It would seem that, if death were due to a *Clostridium welchii* toxemia, the lethal outcome might be deferred or avoided by the administration of sufficient doses of antitoxin. Accordingly, in nine dogs the common bile duct was ligated and the gall bladder defundated and antitoxin was left in the peritoneal cavity. One dog was accidentally strangled in the cage; one lived twenty-nine days, was sacrificed, and a walled-off abscess containing bile-stained pus was found in the right upper quadrant. Six dogs died from thirty-six to forty-eight hours after operation. One lived eight days. All anaerobic cultures (brain broth) from the peritoneal cavity were positive for a gram-positive bacillus resembling *Clostridium welchii.*

TABLE IV

DOG	AMOUNT ANTITOXIN, BRAND	BILE CULTURE	MUSCLE CULTURE	LIVER CULTURE	DEATH	PERITONEAL FLUID	CULTURE PERITONEAL FLUID
8B	15 c.c. Lilly (Welch)	+	−	+	Strang.		
9B	15 c.c. Lilly (Welch)	+	+	−	29 days		
10B	35 c.c. Lilly (Welch)	+	+	+	2 days	600 c.c.	+
11B	15 c.c. Lilly (Welch)	−	+	+	2 days	200 c.c.	+
12B	25 c.c. Lilly (Welch)	−	−	−	2 days	500 c.c.	+
13B	15 c.c. Lilly (Welch)	−	+	+	36 hr.		
14B	30 c.c. Lilly (Welch)	+	−	+	8 days	300 c.c.	+
20B	30 c.c. Lederle	−	−	−	2 days	400 c.c.	+
21B	30 c.c. Lederle	−	−	−	2 days	400 c.c.	+

Three dogs were injected intraperitoneally with antitoxin and sterile dog bile. One lived nine days, one died in twelve to fifteen hours, and one lived fourteen days before being used for another experiment. Controls all died in eight to twenty-four hours. Two dogs were injected with bovine bile in 11.5 c.c. per kilogram of body weight and 8.4 c.c. per kilogram of body weight amounts and mixed antitoxin containing 10,000 perfringens units and 10,000 vibrion septique units. Both dogs died in eight hours.

This antitoxin offered some degree of protection to guinea pigs when they were injected intramuscularly with the anaerobic dog liver organisms in that, although it did not prevent development of gas infection, it decreased its severity and deferred the time of death. In controls the intramuscular injection of cultures of the dog liver anaerobic organism resulted in violent gas infections eventuating in death. This evidence appears to be contrary to the theory of Trusler and Martin[22] that these organisms are nonpathogenic anaerobes producing no exotoxin, and it seems to substantiate the contention of Andrews, Rewbridge, and

Hrdina[1] that the organism is pathogenic and closely related to, if not identical with, *Clostridium welchii.*

Biopsies obtained from the muscles of nine guinea pigs proved sterile on anaerobic culture (brain broth); that from one guinea pig contained staphylococcus, probably a contaminant. Sterile whole bovine bile was injected intramuscularly into ten guinea pigs, in two of which antitoxin was also injected. The affected muscle was cultured upon death; no effect was apparent from the antitoxin in this series.

TABLE V

GUINEA PIG	BILE SALTS INTRAMUSCULARLY	DEATH	GAS	ANTITOXIN	MUSCLE CULTURE
1	1,700 mg.	21 hr.	+	–	Gm. + rods
2	1,700 mg.	23 hr.	+	–	Gm. + rods
3	850 mg.	27-38 hr.	+	–	Gm. + rods
4	850 mg.	123-134 hr.	–	–	Not done
5	1,700 mg.	114 hr.	–	+	Gm. + rods *Str. diplococci*
6	1,700 mg.	43 hr.	–	+	Gm. + rods
7	1,700 mg.	2 hr.	–	–	Not done
8	1,700 mg.	23 hr.	+	–	Gm. + rods
9	1,700 mg.	22 hr.	+	–	Gm. + rods
10	1,700 mg.	39 hr.	+	–	Gm. + rods Staphylococci

In every case in which cultures were taken, the muscle tissue showed gram-positive anaerobes similar in morphology and cultural characteristics to *Clostridium welchii.*

If the devitalizing action of bile salts will bring about an endogenous infection of the peritoneal cavity by *Clostridium welchii* which have been lying dormant in the tissues, an injection of other irritants should bring about the same exodus of *Clostridium welchii* with a resultant toxemia. Accordingly, hypertonic saline solution, dextrose, and hydrochloric acid were injected intraperitoneally into seven guinea pigs and the ascitic fluid subsequently cultured.

Bile therefore must have some more specific action than merely devitalizing the tissues to enable the anaerobic organism to thrive, since all these cultures were sterile. Upon injecting these irritants intramuscularly and subsequently culturing muscle biopsies, variable results were obtained, but in no instance was an organism closely resembling *Clostridium welchii* found.

Since the intraperitoneal injection of irritants other than bile failed to effect the presence of *Clostridium welchii* in the ascitic fluid of these animals, it was thought that a comparison of the post-mortem findings in bile peritonitis with those in animals that had received injections of both *Clostridium welchii* and an irritant might prove illuminating; consequently, a 50 per cent barium sulfate suspension was injected intraperitoneally into eight dogs. Simultaneously pure cultures of *Clostridi-*

TABLE VI

GUINEA PIG	INJECTION, INTRAPERITONEALLY	GM. WEIGHT	KILLED	ASCITES C.C.	CULTURE
11	10 c.c. NaCl 20%—50% glucose	526	2 hr.	30	Sterile
12	10 c.c. 20% NaCl—50% glucose	550	4 hr.	5	Sterile
13	10 c.c. 20% NaCl	450	1½ hr.	30	Sterile
14	10 c.c. 20% NaCl	475	4½ hr.		Sterile
15	10 c.c. 1% HCl	435	16 hr.		Sterile
16	10 c.c. 1% HCl	422	16 hr.		Sterile
17	10 c.c. 20% NaCl	512	1½ hr.	23	Sterile

um welchii were injected intraperitoneally. Four of these dogs died in from fifteen to seventy-two hours. At post mortem were found 50 to 250 c.c. of foul-smelling ascitic fluid which was bloody, darkly hemorrhagic peritoneal and serosal surfaces, essentially the findings of bile peritonitis. Cultures of the ascitic fluid were positive for the Welch bacillus.

The remainder of the dogs, one of which was given 400 c.c. of 6 per cent acacia solution intravenously, were living after several weeks. Two dogs were injected intraperitoneally with 50 per cent glucose solution and Welch culture; both remained living and apparently well.

TABLE VII

DOG	WEIGHT IN KG.	PROCEDURE	SUBSEQUENT COURSE
36	8.2	50 c.c. Ba plus 20 c.c. Welch culture	Living and well
37	9.6	50 c.c. Ba plus 20 c.c. Welch culture	Dead, 3 days
38	10.0	50 c.c. Ba plus 20 c.c. Welch culture	Dead, 25 hr.
39	12.3	50 c.c. Ba plus 20 c.c. Welch culture	Living and well
40	10.0	Ba 5 c.c./kg. plus Welch culture 2 c.c./kg.	Living and well
41	7.5	Ba 5 c.c./kg. plus Welch culture 2 c.c./kg. plus 400 c.c. acacia	Living and well
17	6.8	Ba 5 c.c./kg. plus Welch culture 2 c.c./kg.	Dead, 15 hr.
39	11.3	Ba 5 c.c./kg. plus Welch culture 2 c.c./kg.	Dead 29-40 hr.
36A	7.7	Glucose 2 c.c./kg. plus Welch culture 1 c.c./kg.	Living and well
35	11.2	Glucose 2 c.c./kg. plus Welch culture 1 c.c./kg.	Living and well

The anaerobe alone did not cause death, but apparently did so only when an irritant was given simultaneously.

It is thus seen that bile possesses some specific toxic or devitalizing action, apparently not dependent upon contained Welch bacilli or anaerobes liberated upon escape of bile into the peritoneal cavity. This specific toxic action is quantitative and appears to be due to the bile salt content of the bile.

THE FACTOR OF SECONDARY SHOCK

The remainder of our experimental work was largely directed toward repeating the work of Harkins, Harmon, Hudson, and Andrews,[8, 9] who

contended that death in choleperitoneum is due to shock from loss of plasma-like fluid into the peritoneal cavity; and also to attempt to find an efficacious form of treatment for the condition in experimental animals.

For the first group of experiments to check the findings of Harkins and his co-workers, we used eight apparently normal dogs. Complete anesthesia was induced by the use of sodium pentobarbital; 35 mg. per kilogram of body weight was dissolved in sterile distilled water and injected intravenously. A blood sample was taken at this time and at periodic intervals thereafter; the hemoglobin percentage was determined by a direct colorimetric method suggested by Dr. Frederick Scott. The first dog was prepared and the carotid artery exposed and cannulated, the three-way cannula being connected to a mercury manometer, so that the carotid blood pressure was constantly recorded upon a slowly revolving kymograph. One hundred forty cubic centimeters of sterile bovine bile containing 170 mg. of bile salts per cubic centimeter were injected aseptically into the peritoneal cavity. The carotid blood pressure tracing was continued until death, four hours after the injection of bile.

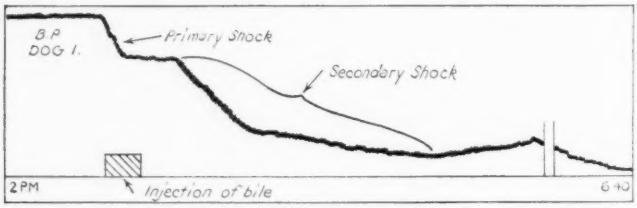

Fig. 1.

At first there was a slight drop in blood pressure, from 180 mm. of mercury mean pressure to 160 mm. Then a more gradual, profound drop to 80 mm. occurred. The blood pressure stayed then for three hours between 40 and 80 mm. of mercury before death occurred.

During this period the hemoglobin percentage rose to 120. At autopsy, 250 c.c. of darkly hemorrhagic ascitic fluid was found and cultured; gram-positive rods and staphylococci were obtained. The peritoneal and serosal surfaces were dull and boggy in appearance. The spleen was very dark, almost black, not enlarged; the liver and kidneys appeared grossly normal; there was no abnormal intravascular clotting; the adrenal cortices were grossly normal, but there were petechiae in the medullas. There was no pleural exudate and the lungs appeared normal. The heart was dilated and flabby. This was essentially the pathologic picture in all of the dogs; there were, however, small pleural exudates in two dogs that had had laparotomies.

In Dog 2 the same procedure was followed and essentially the same results were obtained.

In Dog 3, in addition to the above procedure, 50 c.c. of 30 per cent magnesium sulfate solution was given intraperitoneally with no apparent effect on the course of the condition.

In Dogs 5 and 6 the common bile duct was tied and the gall bladder defundated and the dogs subsequently connected to the kymograph apparatus to record the carotid blood pressure. These dogs survived longer and, with the exception of Dog 3 which had been given hypertonic magnesium sulfate, had relatively the greatest amount of exudate in the peritoneal cavity.

In Dogs 4, 7, and 8, the bovine bile or bile salt solution was injected intravenously a few cubic centimeters at a time. Following each injection, especially if it was made rapidly, there occurred a dip in the blood pressure tracing, each time dropping lower as more bile was injected.

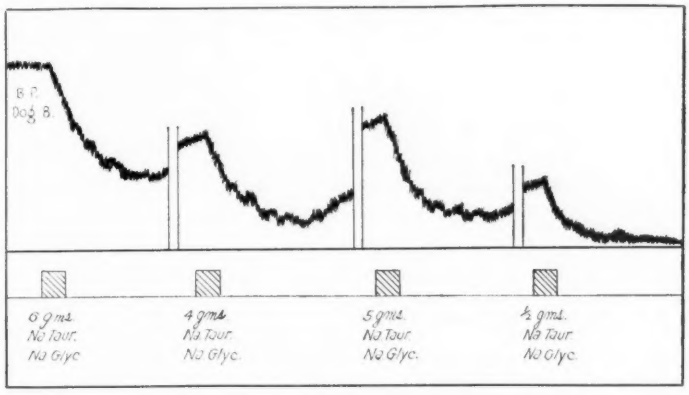

Fig. 2.

The determination of the percentage of blood volume was based upon Welcker's estimation that the blood constitutes 7.7 per cent of the body weight in dogs.[24] It is seen that the dogs having a massive ascites from intraperitoneal irritation have consistently an elevation of hemoglobin percentage indicating hemoconcentration from fluid loss.

The determination of bile salts in the peritoneal exudate was crude and inaccurate, due to the protein content, but, except in the two dogs which were operated upon, it was constantly low, indicating that the intraperitoneal bile was greatly diluted with body fluid. This fluid clotted spontaneously and in all except Dog 5 showed gram-positive rods upon culture. The fluid lost to the circulatory system did not form as great a percentage of the blood volume as most of Harkins, Harmon, and Hudson's cases, and it is doubtful if the loss of this fluid would be sufficient to cause death in itself; however, there is little doubt that it is an extremely important contributing factor in the causation of death in these animals.

TABLE VIII

DOG	PROCEDURE AMOUNT BILE SALTS AMOUNT BILE INJECTED	DEATH IN HOURS	WEIGHT IN KG.	MEAN BLOOD PRESSURE IN MM. HG	HGB. %	AMOUNT PERITONEAL FLUID C.C.	% BODY WEIGHT (FLUID LOST)	% BLOOD VOLUME (FLUID LOST)	BILE SALTS IN PERITONEAL FLUID	CULTURE PERITONEAL FLUID	MISCELLANEOUS PROCEDURES
1	23,800 mg. 140 c.c. ox bile intraperitoneal	4	13.9	182-160-124 90-62-50 64-30	100 110 120	250	0.79	10.4	2.86 mg. 1 c.c.	Staph. gm. + rods	
2	36,330 mg. 230 c.c. ox bile intraperitoneal	8	21.0	166-142-120 140-150-114 106-76-64 48	127 137 137 139 147	450	1.05	13.6	2.58	Staph. Strep. gm. + rods	
3	11,750 mg. 47 c.c. dog bile intraperitoneal	2+	18.6	178-150-140 122-114-132 138-110-80 88-70	128 135 125	360	1.68	21.8	3.62	Strep. gm. + rods	50 c.c. 30% $MgSO_4$ 1 P.
4	18,700 mg. 110 c.c. ox bile intravenous	2+	15.5	168-140-150 90-120-140 62-124-40 64	85.8 78.7	50			0.7	Strep. Staph. gm. + rods	
5	Gall bladder defundated, common bile duct tied and cut	26	27.0	68-52-46	124	370	1.37	17.8	41.0	Strep. Staph.	
6	Gall bladder defundated, common bile duct tied and cut	22	11.4		128	175	1.53	19.9	32.5	Strep. gm. + rods	
7	6,930 mg. 35 c.c. dog bile intravenous	3	22.5	162-120-76 108-76-54 66-52-28	81.6 76.9	None				Strep. gm. + rods	Injected in repeated small doses
8	15,500 mg. 200 c.c. salt solution intravenous	3	23.6	134-60-78-46 78-90-36-48 60-30	94 86	None				Staph. gm. + rods Strep.	Repeated small doses

As controls for this series of experiments, several dogs were placed in the blood pressure apparatus, the carotid cannulated, and various irritant solutions injected intraperitoneally and the blood pressure variations observed.

The primary small drop in blood pressure was always present, but no sustained, profound drop was observed comparable to that occurring when bile or bile salt solution was injected, again indicating the specificity of the action of bile in depressing the circulation. Five grams of glucose in 50 per cent solution, and 140 c.c. of hydrochloric acid in 37 per cent solution were used. At autopsy these dogs had an ascites of varying degree.

TABLE IX

DOG	TIME OF DEATH	INTRAPERITONEAL IRRITANT	BLOOD PRESSURE DROP	HGB. %	PERITONEAL FLUID	CULTURE
9	Killed 4 hr.	Glucose, 5 gm. 50 per cent solution HCl 37 per cent, 140 c.c.	90 mm.	107	200 c.c.	
10	Killed 6 hr.	45 gm. glucose 50 per cent solution	40 mm.	132 138	325 c.c.	
11	Killed 7 hr.	25 gm. glucose 50 per cent solution	30 mm.	125 131	400 c.c.	
12	Died 3½ hr.	50 gm. glucose 50 per cent solution			360 c.c.	Gm. + rods
13	Died 20 days	50 gm. glucose 50 per cent solution				Sterile

The high hemoglobin values and large amount of peritoneal fluid which, however, did not clot spontaneously and was not hemorrhagic, would indicate that shock should be present under these conditions; however, the drop in blood pressure was not great unless massive doses were given and, furthermore, the condition was reversible when moderate doses of the irritant were given; that is, the blood pressure in all the dogs rose to normal following the initial drop.

Eleven dogs were then injected intraperitoneally with bovine bile in amounts of 5 to 10 c.c. per kilogram of body weight. In the last four dogs a skin incision about 1 cm. long was made and the edges retracted; thus the injection was made without touching the skin.

In the others, ordinary sterile technique was used. In the last two dogs, 3 to 4 c.c. of intravenous evipal were used as anesthetic instead of sodium pentobarbital. In three dogs of this series, attempts at treatment were made by supplying fluids in the form of intravenous and subcutaneous physiologic saline solutions and transfusions of blood. In four cases in which the peritoneal effusion was cultured, gram-positive rods were present.

TABLE X

DOG	WEIGHT IN KG.	BILE INJECTED C.C./KG.*	TREATMENT	DEATH	AMOUNT PER FLUID C.C.	% BODY WEIGHT FLUID LOST	% BLOOD VOLUME FLUID LOST	OTHER PROCEDURE
16	9.8	8	100 c.c. saline intravenous 300 c.c. blood intravenous	5 hr.	350	3.5	46.4	
17	6.8	5		Well				
19	10.0	10		6-8 hr.	250	1.5	19.5	
20	11.8	10		4 hr.	200	0.7	9.0	
21	12.7	10	100 c.c. saline intravenous 300 c.c. saline subcutaneous	15 hr.	165	0.3	4.0	
22	12.0	10		2 hr.	150	0.25	3.3	
23	11.5	10		4 hr.	300	1.6	20.5	
24	13.0	10	150 c.c. saline intravenous 100 c.c. blood intravenous	6-15 hr.	320	1.5	19.0	Skin incision
25	14.0	10		6-15 hr.	400	1.85	24.1	Skin incision
26	10.4	7		Well				Skin incision, 3 c.c. evipal
27	13.6	7	200 + c.c. blood intravenous	24-36 hr.	250	1.1	14.8	Skin incision, 4 c.c. evipal

*Bile contained 105 mg. of bile salts per c.c.

If shock due to loss of plasma-like fluid is a factor in the causation of death in bile peritonitis, then the supplying of fluid in sufficient amounts, containing protein comparable in quantity to plasma, might obviate the fatal outcome or alter the disease in some manner; however, it is probable that such fluid should be supplied before the irreversible shock syndrome becomes established in order to get the maximum effect. A series of dogs were treated with intravenous injection of 6 per cent acacia solution (Eli Lilly and Co.) in order to supply a fluid which would not be apt to escape into the tissues. This acacia was given in divided doses, usually spread over a considerable length of time and starting soon after injection of the sterile bile. A parallel series of dogs were used as controls; these animals were given the same dosage of bile as the other dogs, but received no treatment. Intravenous acacia solution was the only therapy any of these dogs received.

Thus it is seen that in the series of dogs with bile peritonitis induced by the injection of sterile ox-bile and left untreated, fourteen dogs died in three to nineteen hours after onset of the condition; one remained living and well, and one died thirteen days after injection.

TABLE XI

UNTREATED DOGS			DOGS TREATED ACACIA			
DOG	BILE/KG. C.C.	DEATH	DOG	BILE/KG. C.C.	6% ACACIA, C.C.	DEATH
43	10	6 hr.	42	10	400	7½ hr.
45	10	7 hr.	44	9	350 250	25 hr.
47	9	6 hr.	46	9	250 350 250	Living
49	9	5-6 hr.	48	9	250 250	18 hr.
51	9	3-4 hr.	50	9	250 250	13-17 hr.
54	8	4 hr.	52	8	250 250 250	Living
55	8	9-19 hr.	53	8	250 250 250	3 days
56	8	5 hr.	57	8	250 250	Living
58	8	Living	60	8	250 250	Living
59	8	13 days	61	8	250 250	Living
62	9	5-12 hr.	63	9	250 250	Living
64	9	3½ hr.	66	9	250	Living
65	9	6 hr.	67	9	250	Living
35	9	2 hr.	41	9	350	Living
36	9	6-8 hr.	57	9	350	Living
40	9	7-19 hr.	58	9	300	Living

Of the dogs which were given acacia solution slowly intravenously, eleven were living several weeks after injection, and five died from seven and one-half hours to three days following the induction of choleperitoneum. This experiment seems to confirm the contention that shock due to fluid loss from the circulatory channels must be a factor in the causation of death in bile peritonitis, and it also indicates the therapeutic value of intravenous isotonic colloid solution in the treatment of this condition in dogs.

CONCLUSION

From our experiments we have concluded that there are at least two factors operative in the causation of death in choleperitoneum; that is, the primary injury to the peritoneum by the toxic bile salts, and the secondary shock from loss of fluid from the vascular system. The toxic effect of absorbed bile and the bacterial factor may be of importance but, if so, they are probably only contributory to the lethal outcome.

REFERENCES

1. Andrews, E., Rewbridge, A. G., and Hrdina, L. S.: Causation of Bacillus Welchii Infection in Dogs by Injection of Sterile Liver Extracts or Bile Salts, Surg. Gynec. & Obst. **53**: 176-181, 1931.

2. Brand, J.: Beitrag zur Kenntnis der Menschlischen Galle, Pflüger's Arch. **90**: 491-520, 1902.
3. Buchanan, J. J.: Bile Peritonitis Without Evident Perforation of the Biliary Tract, Surg. Gynec. & Obst. **26**: 445, 1918.
4. Dvorak, H. J.: Liver Autolysis in the Peritoneal Cavity of the Dog, Proc. Soc. Exper. Biol. & Med. **29**: 431-434, 1932.
5. Fraenkel and Krause: Quoted by Wangensteen.[23]
6. Gregory and Pascoe: Bile Salt Determination, J. Biol. Chem. **83**: 35, 1929.
7. Harkins, H. N., Harmon, P. H., and Hudson, J. E.: Lethal Factors in Bile Peritonitis; "Surgical Shock," Arch. Surg. **33**: 576-608, 1936.
8. Harkins, H. M., Harmon, P. H., and Hudson, J. E.: Peritonitis Due to Bile and to Liver Autolysis, J. A. M. A. **107**: 948-953, 1936.
9. Harkins, H. M., Harmon, P. H., and Andrews, A.: Mechanism of Death in Bile Peritonitis, Proc. Soc. Exper. Biol. & Med. **32**: 691-693, 1932.
10. Horrall, O. H.: Experimental Bile Peritonitis and Its Treatment in the Dog, Arch. Int. Med. **43**: 114-128, 1929.
11. Horrall, O. H.: The Toxicity of Bile, Physiol. Rev. **11**: 122, 1931.
12. Horrall, O. H., and Carlson, A. J.: The Toxic Factor in Bile, Am. J. Physiol. **85**: 591, 1929.
13. McWilliams, C. A.: Acute Spontaneous Perforation of the Biliary System Into the Free Peritoneal Cavity, Ann. Surg. **55**: 235, 1912.
14. Moon, V. H., and Morgan, D. R.: Shock in Bile Peritonitis, Proc. Soc. Exper. Biol. & Med. **34**: 743-747, 1936.
15. Noetzel, W.: Experimentelle Untersuchungen zur Gallenblasen Perforations Peritonitis, Arch. f. klin. Chir. **93**: 160, 1910.
16. Orth, O.: Casuistischer und experimenteller Beitrag zur Leber und Gallengangsruptur, Arch. f. klin. Chir. **101**: 369, 1913.
17. Rewbridge, A. G.: Etiological Role of Gas Forming Bacilli in Bile Peritonitis, Surg. Gynec. & Obst. **52**: 205-211, 1931.
18. Rewbridge, A. G., and Hrdina, L. S.: The Etiological Role of Bacteria in Bile Peritonitis; an Experimental Study in Dogs, Proc. Soc. Exper. Biol. & Med. **27**: 528-9, 1930.
19. Ritter, C.: Die Gallige Peritonitis ohne Perforation, Arch. f. klin. Chir. **118**: 54, 1921.
20. Rywosch, D.: Quoted by Horrall.[11]
21. Sich, C., and Fraenkel, E.: Ein Beitrag zur sog. Galligen Peritonitis, V. Bruns Beitrage **85**: 687, 1913.
22. Trusler, H. M., and Martin, H. E.: Cause of Death in Liver Peritonitis, SURGERY **1**: 243-254, 1937.
23. Wangensteen, O. H.: On the Significance of the Escape of Sterile Bile Into the Peritoneal Cavity, Ann. Surg. **84**: 691-702, 1926.
24. Welcker: Quoted by Starling: Human Physiology, Philadelphia, 1933, Lea and Febiger, p. 687.

SUBPHRENIC ABSCESS

A Medical Review

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NOT INFREQUENTLY, especially in hospital practice, the physician or surgeon is called upon to make or disprove the diagnosis of subphrenic abscess. With few exceptions this is a difficult problem and the diagnosis is often doubtful until pus is found at operation in the subphrenic space. As a means of studying this disease, a review has been made of the 59 proved cases of subphrenic abscess which have occurred in the Toronto General Hospital during a ten-year period since Jan. 1, 1927. Of these 59 cases, 52 were public ward cases and 7 were private cases.

ETIOLOGY

All the subphrenic abscesses of this review had their primary source in the abdominal or pelvic cavities. They occurred following:

Table I

1. Appendicitis	19 cases	(32 per cent)
a. with localized peritonitis or abscess	13 cases	
b. with generalized peritonitis	6 cases	
2. Perforated duodenal ulcer	14 cases	(24 per cent)
a. proved cases	11 cases	
b. unproved cases	3 cases	
3. Perforated gastric ulcer	3 cases	(5 per cent)
4. Perforated gall bladder	2 cases	(3 per cent)
5. Upper abdominal operation on stomach and gall bladder	12 cases	(20 per cent)
6. Pelvic inflammation	4 cases	(7 per cent)
7. Colectomy, right side	1 case	(2 per cent)
8. Perforated large bowel (amebic dysentery)	1 case	(2 per cent)
9. Unknown	2 cases	(3 per cent)
10. Undetermined (private case)	1 case	(2 per cent)

These figures are in agreement with those of other investigators[1, 2] in that lesions of the appendix and perforated gastric and duodenal ulcers accounted for the majority of the cases. Little mention is made in the literature of subphrenic abscesses which have arisen following upper abdominal operations on stomach and gall bladder. But in our series this was a relatively common primary source of infection; 20

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per cent of the cases followed such operations. A probable explanation for this increase is the larger number of upper abdominal operations performed in recent years. Subphrenic abscess arose from the pelvis in four cases, the primary cause being pelvic cellulitis, pelvic peritonitis following miscarriage, abdominoperineal resection of the rectum, and repair of cystocele and rectocele.

Cases of subphrenic abscess which have arisen from a primary source in the thorax have been reported in the literature.[3, 4] Most of these have been due to empyema, basal lung abscess, or bronchiectasis. Septicemia, which was present in a few of our cases, has been cited[1, 3] as a source from which infection has reached the subphrenic space. However, none of the subphrenic abscesses of this review arose either from the thorax or from a septicemia.

LOCATION

Accurate anatomic descriptions of the subphrenic spaces have been given by Martinet[5] and Barnard.[6] In his excellent paper Barnard depicts the subphrenic region as being divided on each side into three sections, and, according to the relationship of each section to the peritoneum, they are termed the anterior and posterior intraperitoneal spaces and the extraperitoneal space. Most writers on the subject of subphrenic abscess have made use of this classification. However, it was not used in this study since, in many of our cases, it was impossible to localize the abscess with sufficient accuracy, even after operation. This is to be expected since in surgical drainage the subphrenic abscess was opened usually from its most accessible site, and it was neither possible nor advisable to determine its entire extent.

In this review subphrenic abscesses have been classified for practical purposes according to their relationship to an imaginary line drawn in the coronal plane of the body through the dome of the diaphragm. A line so drawn will divide the subphrenic space into two parts on each side. Abscesses situated mainly anterior to this line and pointing anteriorly were designated as "anterior." Similarly, those which were situated mainly posterior to this line and pointing posteriorly were classified as "posterior." In several cases the abscesses were centered mainly on this imaginary line or under the dome of the diaphragm and these have been designated as "dome." In a few cases the abscesses were so extensive as to be posterior, anterior, and dome; these have been termed "massive." Massive in this instance refers to the extent of the abscess rather than to the quantity of pus it contained.

According to this classification, the location of subphrenic abscesses in the 59 cases reviewed was as follows:

TABLE II

	ANTERIOR	POSTERIOR	DOME	MASSIVE	UNDETERMINED LOCATION	TOTAL
Right side	13	17	10	2	2	44
Left side	2	2	3	2	2	11
Bilateral						2
Undetermined						2

In this series of cases subphrenic abscesses arising from disease of the appendix were usually located posterior, while those arising from lesions of upper abdominal organs were more frequently anterior or dome abscesses. Lesions of the appendix, gall bladder, and duodenum caused 80 per cent of the subphrenic abscesses occurring on the right side. Abscesses from lesions in these organs rarely occurred on the left side and, when they did occur, were usually associated with a generalized peritonitis. Left-sided subphrenic abscesses were most frequently caused by lesions of the stomach, such as perforated gastric ulcer, or following gastrectomy.

SYMPTOMS

Symptoms were recorded in 36 of the 52 public ward cases. In the remaining 16 cases the records were too incomplete for careful analysis as far as symptomatology was concerned. The general symptoms produced by subphrenic abscesses, such as weakness, sweating, loss of appetite, vomiting, occasionally chills, etc., are too variable and too commonly associated with suppurative conditions elsewhere in the body to be of any real value in localizing the infection to the subphrenic space.

The local symptoms found in this series were of great value in directing attention to the subphrenic space as the site of the inflammatory process. Pain of various types was the most important of these symptoms. Pain of at least one type was present in 33 of the 36 cases. Pleural pain was noted in 11 cases. It was present in the lower chest and usually most marked laterally. It tended to be of relatively short duration, lasting in most cases not longer than a week. Shoulder-tip or diaphragm pain occurred in 7 cases and was usually an early symptom and transient in character. Aching pain in the lower chest or along the costal margin was recorded in 16 cases. It appeared as a later symptom and, once present, usually remained until the abscess was drained. Pain in the upper quadrant was observed in 7 cases, in all of which the abscesses were located on the right side. In 3 of these 7 cases the abscesses were anterior and extended as a mass in the right upper quadrant from under the costal margin. Pain in the flank was present in 3 cases, 2 of which were of posterior abscesses, the other a dome abscess. This pain was aching in character and tended to remain until drainage was established.

Cough proved to be a difficult symptom to evaluate since most of the patients with subphrenic abscess had had operations for the primary condition, frequently done under general anesthesia. Many of these patients had cough postoperatively for several days, often due to either bronchopneumonia or postoperative collapse. In such instances the cough could not be attributed to or definitely related to the subphrenic abscess. In 6 cases, however, the cough was present when the abscess was well developed and appeared to be related to the subphrenic abscess. The cough was unproductive in 1 of these cases and productive in 5. The sputum was small in amount, mucoid in 3 and mucopurulent in 2 cases. Compression or basal collapse of the lung was the likely cause of the sputum and cough.

Hiccough, which other investigators[2, 7] have commonly found, was noted in only 2 of our cases. In 1 it proved to be very distressing and was present continuously for twelve days.

PHYSICAL SIGNS

These were recorded accurately in 46 cases and may be divided into those chiefly found in the thorax and those chiefly abdominal.

A. *Thoracic Signs.*—The most common physical finding was impaired resonance in the lower chest. This usually went as high as the inferior angle of the scapula posteriorly, and tended to extend anteriorly into the axilla and to a slightly lower level in the anterior chest. This more or less horizontal area of impaired resonance was present in 38 of the 46 cases (82 per cent). In this area of impaired resonance tactile fremitus was absent and the breath sounds decreased in intensity in all cases. The breath sounds were absent in 10 cases, diminished in 19, decreased bronchovesicular in 2, and distant bronchial in 6. At the upper part of this area of impaired resonance and decreased breath sounds, râles were recorded in 8 cases (17 per cent). A pleural friction rub was also heard in 7 cases (15 per cent). This was a relatively early finding and did not last longer than one week. Shifting dullness and succussion splash were found in the lower chest in 1 case only, where fluid and air were present in the subphrenic abscess. An unusual sign observed in 1 case in which the subphrenic abscess had been present for two years was clubbed fingers.

B. *Abdominal Signs.*—Tenderness in the right upper abdominal quadrant was present in 7 cases, in 6 of which the abscess was anterior while in the seventh it was posterior. In 3 of these cases a mass was found in the right upper quadrant, indicating the position of the abscess. Tenderness in the costovertebral angle was present in 6 cases, 4 of which were posterior abscesses but 2 were anterior abscesses. Subcutaneous edema also was present in the costovertebral angle and around the flank in only 3 cases. Downward displacement of the liver was recorded in only 4 cases.

Diminished movement of the chest, impaired resonance, and altered breath sounds are the common triad of signs in cases of subphrenic abscess. The latter two occurred in more than 80 per cent of this series of cases.

VALUE OF PHYSICAL SIGNS IN LOCALIZATION

Efficient surgical drainage is a necessity in the successful treatment of a subphrenic abscess. Such efficient drainage is greatly facilitated by a knowledge of the maximum location of the abscess. Signs helping to localize the abscess as anterior were: first, the signs of impaired resonance, etc., found in the chest were higher anteriorly than posteriorly in 8 out of 15 cases of anterior abscess; second, in 4 cases of the 15 anterior abscesses tenderness was present anteriorly and in 3 of these a mass could be felt in the upper abdomen. However, all anterior abscesses had physical signs posteriorly, and in many cases physical signs were of little value in determining the maximum location of the subphrenic abscess.

FEVER

Temperature readings taken at the time of diagnosis, or a few days before death where clinical diagnosis was not made, have been compiled in 48 cases in which the subphrenic abscess was considered to be the dominant condition present. Of this group, 86 per cent had a well-marked elevation of temperature (over 101° F.); 10 per cent had slight elevation (under 100° F.); and in 4 per cent there was a normal temperature. The fever generally was remittent or intermittent in character and the temperature charts tended to fit into two types: (1) a group of cases which had a low grade temperature postoperatively for five to ten days, then a gradual elevation of temperature which became swinging or septic in character; (2) a group of cases having high fever postoperatively which continued or increased and became septic in type.

LEUCOCYTE COUNT

The leucocyte counts were estimated in 37 cases within a few days of the time the subphrenic abscess was proved. In 70 per cent of these cases a leucocytosis was present with a count of over 12,000 white blood cells per cubic millimeter: the majority of these were over 15,000. Approximately 25 per cent of the cases had leucocyte counts under 11,000 and in 2 cases the count was normal. It is significant that each of these cases with normal leucocyte counts had a temperature of 102° F.

X-RAY EXAMINATION

X-ray films or fluoroscopic examinations were made use of in 36 of the 52 public ward cases. The variability of the findings is well illustrated by Table III.

TABLE III

X-RAY FINDINGS	NO. OF CASES	PERCENTAGE
High diaphragm (no record of movement)	15	42
Diaphragm high and fixed	8	22
Diaphragm high with restricted movement	4	11
Diaphragm, normal position; no record of movement	2	6
Diaphragm in normal position with diminished movement (right anterior lateral)	1	3
Diaphragm moving freely; no record of its position (right anterior lateral)	1	3
Diaphragm not visualized, due to pleural effusion	5	14
In the above cases gas and fluid were found beneath the diaphragm: perforated ulcer, 5; gastrectomy, 2; appendicitis, 1	8	22

In this series of cases subphrenic abscess occurred when the diaphragm was in normal position or when it had normal movement, but in no instance were both these findings present together. It is seen from the above figures that x-ray examination is of definite value as an aid to history and physical examination in the diagnosis of subphrenic abscess.

THORACIC COMPLICATIONS

Of all the complications of subphrenic abscess, those occurring in the thorax are the most frequent and are very likely to cause serious or fatal consequences. In 45 subphrenic abscesses the thoracic complications have been listed in their order of frequency.

Pleural Effusion.—A pleural effusion occurred in 14 cases (31 per cent). Of itself it was not serious, but greatly increased the difficulty of diagnosing the subphrenic abscess and in 9 of the 14 cases an empyema developed. A pleural effusion was not necessarily a late complication. This was shown by the fact that 3 cases developed an effusion within a week of the probable onset of the subphrenic abscess. The development of pleural effusion following an infective lesion in the abdominal cavity, especially relating to stomach, gall bladder, duodenum, or appendix, should demand that the possibility of a subphrenic abscess be considered.

Rupture into Lung and Bronchus.—This was a serious and usually fatal complication. It happened in 6 cases (13 per cent), and in only 1 case did recovery take place. In 5 instances it occurred on the right side and in 1 case on the left. Lung abscess developed in 3 cases and a septic pneumonia in another. Rupture into a bronchus was largely a late complication and, with the exception of 1 case in which it took place in ten days after the probable onset of the subphrenic abscess, always occurred after forty days, or later, in 1 case two years. The case in which rupture occurred in ten days demonstrates the fact that diagnosis of subphrenic abscess should be made early in order that this complication may be avoided. That adequate drainage is also essential in preventing this complication was illustrated by one case in

which the abscess was drained within twenty-six days, but two weeks later ruptured into a bronchus. The drainage had been inadequate.

Rupture into Pleural Cavity.—This complication developed in 6 cases (13 per cent), and these do not include 2 cases in which a small amount of pus spread into the pleural cavity when a subphrenic abscess ruptured into a bronchus. Rupture into the pleural cavity, on the average, is an earlier complication than rupture into a bronchus. In 5 cases in which accurate dates were available, it took place between fourteen and thirty-five days after the onset of the abscess.

DIAGNOSIS

The duration of the subphrenic abscess from the probable time of onset to diagnosis has been recorded in 51 cases in which accurate dates were available. The two shortest time intervals were in subphrenic abscesses due to perforated duodenal ulcers and were five and eight days. The longest duration was two years in a case in which the primary cause was probably a perforated duodenal ulcer. Thirty-nine of the 52 public ward cases were correctly diagnosed, and of these the average time to diagnosis was twenty-seven days. Many of these cases required relatively long periods of observation to exclude other diagnoses before the true nature of the condition was recognized.

Thirteen public ward cases were incorrectly diagnosed. In 12 of these accurate dates were available and the average duration from onset to diagnosis, by autopsy or fatal complication, was forty days. These 13 cases were divided into two groups, as follows:

1. Subphrenic abscess was undiagnosed in 7 cases, or not diagnosed until within a few days of death when some complication developed which made the correct diagnosis apparent. Four of these abscesses ruptured into lung and bronchus; 1 ruptured into the pleural cavity. Two cases had other fatal infections; 1, septicemia; and 1, pyelophlebitis.

2. In 6 cases the diagnosis was incorrectly made and proved at postmortem examination or operation to be a subphrenic abscess. Of these 1 case was diagnosed as collapsed left lower lobe; 2 were diagnosed as pleural effusion. In 1 of the latter a pleural effusion was found secondary to a subphrenic abscess, and in the other case no pleural effusion was present. Three cases were diagnosed as empyema. In 2 of these the pleural cavity was normal; in the third an effusion was present secondary to a subphrenic abscess.

All of these 13 cases terminated fatally. In 9 of them a fatal outcome might have been avoided by an early and correct diagnosis.

Diagnostic Aspiration.—Aspiration through the diaphragm as a method of diagnosing subphrenic abscess has been advocated and condemned by various writers for many years. In 7 of our cases a needle was inserted either accidentally or intentionally through the diaphragm. In 6 cases pus was found, but in the seventh case a negative result was

obtained from an aspiration done posteriorly. Later, a subphrenic abscess was drained anteriorly in this case. One case developed empyema of the pleural cavity following, and possibly due to, diagnostic puncture.

The presence of subphrenic abscess which was not found by diagnostic aspiration and the possible production of an empyema of the pleural cavity show the unreliability and danger of this method of examination. In our opinion it should never be used with one possible exception; that is, in an extremely ill patient where an incorrect diagnosis of subphrenic abscess with a resulting unnecessary operation might be fatal. Under these circumstances it may be wise to do a diagnostic aspiration, but it should be done on the operating table and, if pus is found, surgical drainage of the abscess undertaken at once. With this possible exception, diagnostic aspirations should not, in our opinion, be undertaken.

MORTALITY

The total mortality of the 59 cases in this series was 28, 47 per cent. This figure is not strictly representative of the mortality of subphrenic abscess alone, since 10 of the 28 fatal cases had one or more of three associated conditions; namely, septicemia, generalized peritonitis, multiple abdominal abscesses. In these 10 fatal cases the subphrenic abscess was not likely or necessarily the primary cause of death. If these 10 cases are excluded from the series, the mortality of the cases in which a subphrenic abscess was the primary cause of death is 31 per cent.

Thirty-nine cases of subphrenic abscess in this series were operated upon for drainage of the abscess. Of these, 9 died, giving an operative mortality of 23 per cent. This operative mortality is not applicable to subphrenic abscess as the predominant condition, since 4 of the 9 fatal cases had associated conditions which were equal or greater factors in the cause of death. Two of the cases had septicemia and 2 had multiple abdominal abscesses. If these 4 cases are removed from the statistics, the operative mortality of the cases in which a subphrenic abscess was the primary cause of death becomes 13 per cent.

DISCUSSION

Subphrenic abscess presents a most difficult problem in diagnosis. This is shown by the number of cases incorrectly diagnosed and by the length of time required to make a correct diagnosis. Often associated with late diagnosis is the development of serious complications, most of which are related to the thorax. Rupture into the lung and pleural cavity are relatively frequent events where diagnosis is delayed.

After a review of these cases, it seems imperative to direct attention to earlier diagnosis. The value of a careful history and thorough physical examination cannot be stressed too greatly in a consideration of this disease. Any infective or suppurative lesion in the abdomen or pelvis, especially if it is associated with free infected fluid, may be

a primary source of infection resulting in a subphrenic abscess. Special attention should be given to lesions of the duodenum, stomach, gall bladder, and appendix, since lesions of these organs account for such a high percentage (84 per cent) of the cases.

CONCLUSIONS

1. All 59 cases of subphrenic abscess reviewed had a primary source in the abdomen or pelvis; 84 per cent originated from lesions of the duodenum, appendix, stomach, and gall bladder; 7 per cent arose from the pelvis.

2. In 75 per cent of our cases the abscess was located on the right side; 19 per cent were on the left side; 3 per cent were bilateral; and in 3 per cent of the cases the position was undetermined. The abscess was posterior in 32 per cent of the cases; anterior in 25 per cent; over the dome of the diaphragm in 22 per cent; and in 7 per cent of the cases it was massive, involving all regions of the subphrenic space.

3. Lesions of the appendix, gall bladder, and duodenum caused 80 per cent of the subphrenic abscesses occurring on the right side. Left-sided subphrenic abscesses were most frequently caused by lesions of the stomach, such as perforated gastric ulcer or following gastrectomy.

4. Lesions of the appendix caused most of the posterior abscesses, while lesions of the duodenum and gall bladder were the primary cause of the majority of anterior abscesses.

5. The commonest and most important symptom pointing to a subphrenic abscess was pain. Cough and sputum appeared to be of little value in diagnosis.

6. The most common thoracic findings were diminished movement, altered tactile fremitus, impaired resonance in the lower chest, and altered breath sounds. The last two findings were noted in over 80 per cent of this series.

7. Physical findings in the abdomen were much less common than those found in the chest. Tenderness in the upper abdomen was present in 9 per cent, while a mass could be felt in 6 per cent. Costovertebral tenderness was found in 13 per cent and subcutaneous edema in only 6 per cent. The liver was found displaced downward in only 9 per cent of the cases.

8. It was difficult to localize the abscess either anteriorly or posteriorly in many cases. Thoracic signs were more prominent anteriorly than posteriorly in 53 per cent of cases where the abscess was anterior. In all abscesses, thoracic signs were present posteriorly. Abdominal signs in the right upper quadrant occurred in anterior abscesses as follows: tenderness in 26 per cent; a palpable mass in 20 per cent.

9. X-ray examination, including fluoroscopy, was a valuable aid to diagnosis. A high diaphragm, either fixed or with restricted movement, was found in 75 per cent of the cases.

10. Diagnostic aspiration of the subphrenic space should seldom be done.

11. Pleural effusion occurred in 31 per cent of the cases; empyema of the pleural cavity in 15 per cent; rupture of abscess into a bronchus in 13 per cent; rupture into the pleural cavity in 13 per cent.

12. The mortality in all cases where the subphrenic abscess was the primary cause of death was 31 per cent. The mortality of the cases operated upon was 13 per cent.

13. Earlier and more accurate diagnoses could have materially reduced this mortality rate.

REFERENCES

1. Ochsner, A.: Subphrenic Abscess, Ann. Surg. **98**: 962, 1933.
2. Dexter, R.: Diagnosis of Subphrenic Abscess, Am. J. M. Sc. **170**: 810, 1925.
3. Barnard, H. L.: Surgical Aspects of Subphrenic Abscess, Brit. M. J. **1**: 429, 1908.
4. Archibald, E.: Discussion of Beye's Paper, Arch. Surg. **14**: 260, 1927.
5. Martinet: Des Variétés anatomique et d'abcès sous phrenique, Thesis of Paris, 1898.
6. Barnard, H. L.: Surgical Aspects of Subphrenic Abscess, Brit. M. J. **1**: 371, 1908.
7. Lockwood, A. L.: Subdiaphragmatic Abscess, Surg., Gynec. & Obst. **33**: 507, 1921.

THE PALMAR FASCIA IN CONNECTION WITH DUPUYTREN'S CONTRACTURE

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THE study of the palmar fascia was undertaken with the intention of throwing more light on the cause of flexion deformity of the fingers observed in Dupuytren's contractures. In reviewing the literature it was found that the description of the palmar fascia with all its dependencies was not always very clear and varied a great deal in textbooks.

The present study was mainly based on multiple dissections of hands in different age groups and on review of literature.

The palmar aponeurosis is an irregular triangular sheet found under the skin of the palm of the hand; its base is directed toward the metacarpophalangeal joints; its apex is continued with the tendon of the palmaris longus, in cases where the palmaris longus is present. According to LeDouble, the palmaris longus is absent in 11.2 per cent of subjects. When the palmaris longus is absent, the apex of the palmar aponeurosis is found at various levels of the wrist, adhering either to the annular ligament or to the antibrachial fascia. The palmar fascia is limited externally by the thenar and medially by the hypothenar aponeurosis. These last structures are much thinner than the central portion. The palmar aponeurosis consists of longitudinal and transverse fibers.

LONGITUDINAL FIBERS

The longitudinal fibers have a double origin. The more superficial and more abundant fibers continue the palmaris longus tendon. The deeper longitudinal fibers continue the annular ligament. These last fibers have an oblique direction and form two groups; one group goes from the medial part of annular ligament toward the metacarpophalangeal joint of the index finger. The other group, coming from the lateral side of the annular ligament, is going toward the metacarpophalangeal joint of the fifth finger. Thus, these two groups cross in the form of a letter X and are situated directly under the superficial longitudinal fibers (see Figs. 1 and 4). The superficial longitudinal fibers form a divergent sheet of uneven thickness. Over the flexor tendons of the second, third, fourth, and fifth fingers the sheet is more dense and forms four bands. These bands were named pretendinous bands by Legueu and Juvara, who gave an excellent description of the fascia of the hand in 1892. These pretendinous bands may vary in num-

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ber. In an article published recently by Kalberg, the number of pretendinous bands was found very variable; instead of the usual four, he found five, six, and seven. He also found that the number of these bands may differ in the hands of the same individual. Between the pretendinous bands are found the intertendinous bands which are less dense. The fibers of the intertendinous bands are intimately connected

Fig. 1.—Four pretendinous bands are shown with digital prolongations forming two lateral bands around the proximal phalanx. The digital vessels and nerves are usually covered by these bands; they are also covered by the thin superficial transverse ligament and are only visible for a short distance in the spaces between the pretendinous bands. The oblique fibers crossing in the form of a letter X are seen emerging from the sides of the palmar fascia. The superficial transverse ligament is shown proximal to the ligamentum natatorium. They are both represented denser than seen in reality.

with the skin of the palm of the hand. The termination and insertion of the pretendinous bands is complex and can be divided into three distinct groups.

First Group.—The fibers of the first group go to the deep surface of the skin of the palm along the entire length of the pretendinous bands;

they are especially marked over the metacarpophalangeal joints. Some of these fibers are attached to the proximal and middle phalanges of the fingers on their volar surface and also on the lateral side, forming two distinct lateral bands (see Fig. 1). These bands are described by several anatomists and are illustrated well by Frazer in *The Anatomy of the Human Skeleton*. They were also noticed by Dupuytren. However, these bands are not constant. It should be mentioned here that the attachment of these bands to the phalanges apparently gave reason to consider the palmar aponeurosis as a terminal tendon of the palmaris longus and as a remnant of a subcutaneous flexor of the fingers. This last view is contested. M. Ferrarini, of the Anatomical Institute of the University of Pisa, found that the palmaris longus is of a very late phylogenetic development and that the various structures of the palmar fascia are not a uniform embryological entity.

Second Group.—The second group of fibers is directed toward the deep interosseous fascia. They encircle the flexor tendons, forming regular

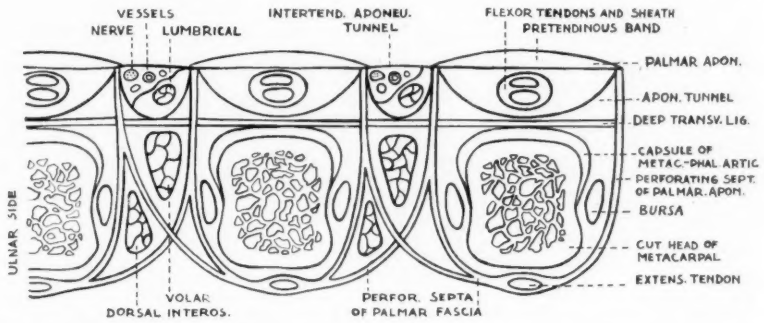

Fig. 2.—Redrawn and modified from Legueu and Juvara. Schematic cross section of the hand through the metacarpal heads to show the arrangement of the third group of perforating fibers of the longitudinal pretendinous bands.

tunnels for the tendons. Similar and separate tunnels are formed around the lumbricals and the digital nerve and vessels. These tunnels are found only under the middle third of the palmar fascia between the distal border of the ulnar bursa and the deep transverse ligament. These tunnels are of unequal length, the longest one surrounding the flexor tendon of the index finger and the shortest surrounding the fourth finger. The little finger usually has no tunnel, the length of the tunnels being dictated by the length of the flexor tendons which are not covered by the sheath of the ulnar bursa distally and the digital bursae of the fingers. The volar surface of the ulnar bursa intimately adheres to the palmar aponeurosis in its proximal third and over the flexor tendon of the little finger (see Fig. 5).

Third Group.—The third group of fibers are called the perforating fibers. They can be observed only over the heads of the metacarpals; detached from the borders of the deep surface of the pretendinous bands, they are directed straight downward from the palm of the hand to the

dorsum between the metacarpal heads (see Fig. 2); they perforate the deep transverse ligament, form separate sheaths for the interosseous muscles, and surround the head of the metacarpals on both sides, becoming connected with the dorsal aponeurosis of the hand. While passing between the metacarpal heads, they do not adhere to the periosteum of the metacarpal head. They are sometimes separated from the periosteum by a small bursa. This is frequently observed in children. It is well known that the palmar aponeurosis is separated from the thenar and hypothenar aponeuroses. There exists between the radial border of the palmar aponeurosis and the thenar aponeurosis a dense septum which is attached to the volar crest of the third metacarpal and which separates the thenar muscles and forms the lateral border of the middle palmar space. This septum is so constructed in certain cases that the flexor tendons of the index with the first lumbrical are left within the thenar space, being in a more or less intimate connection with the adductor of the thumb. DeLorme has given a description of this area. The investigations of Kanavel showed that clinically this is more frequently observed than the other anatomical arrangement in which the flexor tendons of the index are wholly within the midpalmar space. On the ulnar side, a much thinner septum is present between the hypothenar muscles and the ulnar border of the aponeurosis. This septum, attached to the anterior crest of the fifth metacarpal, separates the ulnar side of the middle palmar space from the thenar muscles.

TRANSVERSE FIBERS

The transverse fibers of the palmar aponeurosis are situated under the longitudinal fibers and are more developed at the distal part of the palmar aponeurosis. Over the metacarpal heads a real transverse ligament can be observed. Poirier named this ligament, by analogy to the deep transverse ligament, the superficial transverse ligament of the hand. This ligament has no distinct proximal border but is very distinctly separated distally and forms a visible border about 1 cm. proximal to the webs of the fingers. In the area just below the webs of the fingers Grapow described a structure which he named the "ligamentum natatorium" (see Fig. 1). The superficial transverse ligament is extended from the external tubercle of the second metacarpal head to the internal tubercle of the fifth metacarpal head. Certain fibers go around these metacarpal heads and may become attached to the extensor tendons; shorter fibers extend over the intertendinous spaces of the palmar aponeurosis only. The ligamentum natatorium is thus described by Poirier: "Its proximal border is transverse and is very distinctly separated from the distal border of the superficial transverse ligament; between the two borders there is a distance of at least 1 cm. The distal border of the natatory ligament corresponds to the volar surface of the phalanges and to the web spaces. This ligament is constituted by

a number of short and long fibers which extend from one finger to another and which are attached to the fibrous sheaths of the fingers or to the deep surface of the skin of the fingers; other fibers are in continuation with the longitudinal digital prolongations of the palmar aponeurosis; according to Frohse the natatory ligament limits the flexion of a finger when the nearest fingers are in extension."

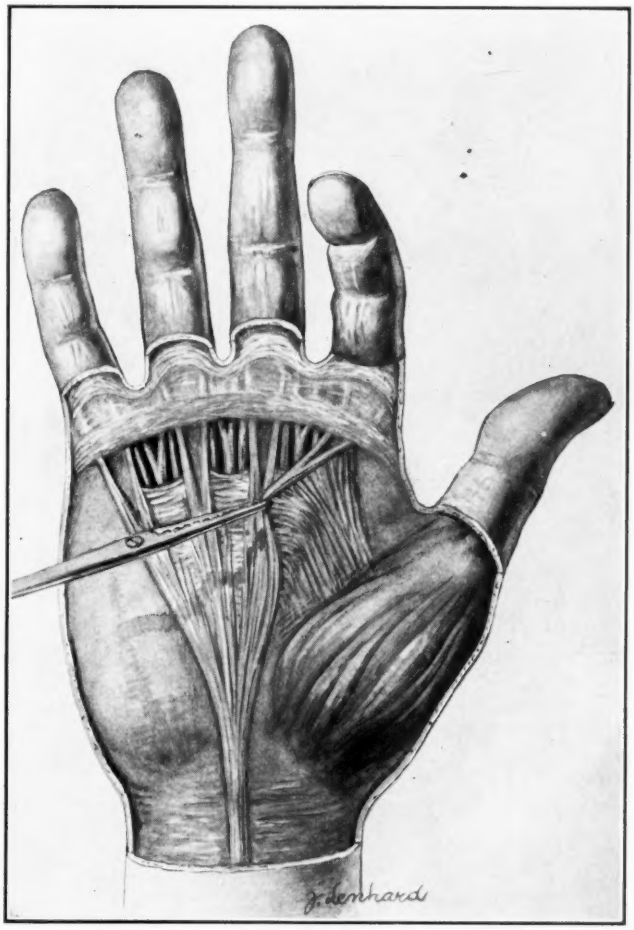

Fig. 3.—Palmar fascia after removal of skin. The ligamentum natatorium and the superficial transverse ligament are shown. Traction on the pretendinous band of the index finger shows flexion of the proximal and middle phalanges.

It is generally considered that for the successful treatment of Dupuytren's contracture it is necessary to remove the entire palmar fascia, including the penetrating septa which form tunnels around the tendons, nerves, vessels, and lumbrical muscles of the hand. However, numerous surgical observations in patients afflicted with Dupuytren's contractures indicated that the contracture of the palmar aponeurosis did not extend down to the subaponeurotic expansions (to the second and third group of fibers as described above).

To investigate this problem, the following experiments were carried out: A careful dissection of the palmar skin was done, separating it from the palmar aponeurosis up to the web of the fingers. The skin was reflected and the palmar aponeurosis was carefully exposed but was left intact. With the fingers held in extension, each pretendinous band was grasped separately with a forceps and pulled in a proximal direction.

Fig. 4.—The palmar fascia separated from the underlying structures and lifted up shows on the undersurface the oblique fibers. The traction on the pretendinous band shows the flexion of the proximal and middle phalanx.

The pulling invariably produced a slight flexion of the corresponding proximal and sometimes proximal and middle phalanges (see Fig. 3). In those cases where the pulling of the pretendinous bands did not produce a flexion of the proximal phalanx, it was observed that no trace of a digital prolongation of the pretendinous band could be found. A similar traction of the dissected and reflected skin, in the axis of the fingers, never produces a flexion of the corresponding fingers. Subsequently,

the palmar fascia which was previously dissected from the skin was very carefully dissected from the underlying structures: the annular ligament, tendons, lumbrical muscles, and vessels. The deep extensions of the palmar aponeurosis going toward the interosseous fascia were not excised. The palmar fascia was lifted up but was left attached by its base distally. Each pretendinous band was grasped on its deeper surface with a forceps and pulled in the same direction as in the previous

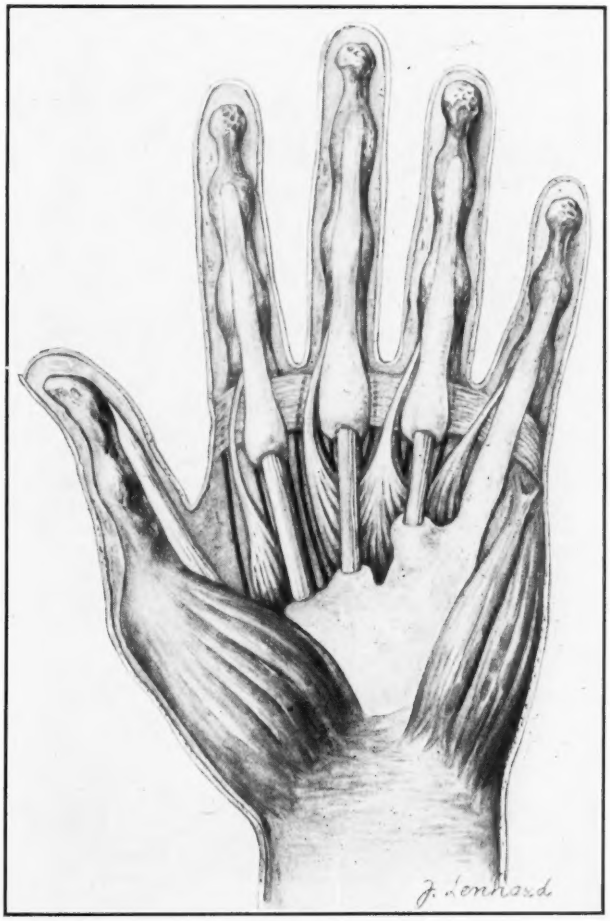

Fig. 5.—The schematically shown heavy black lines between the tendons show how the second group of the pretendinous bands penetrate between the tendons and also show their unequal length. The heavy black line between the index and medius shows the separation of the midpalmar space from the thenar space.

experiment. It was found that the traction produced a strong flexion of the corresponding proximal phalanx (see Fig. 4). This experiment was repeated on several hands and produced positive results invariably, except in those cases where no digital prolongations could be found (first group of fibers). On the basis of this study, it was concluded that the flexion contracture of the fingers which is observed in the Dupuytren's syndrome is probably due almost exclusively to the contracture of the

phalangeal insertions of the pretendinous hands of the palmar aponeurosis and has little or nothing to do with the deep extensions of the palmar aponeurosis toward the deep interosseous fascia. It may be suspected that Dupuytren's syndrome may develop only in those cases where the digital prolongations of the pretendinous bands are present.

SUMMARY AND CONCLUSION

A study of the palmar fascia was made with the intention of discovering which part of the palmar aponeurosis is mostly responsible for the flexion contracture of the fingers. It was found that only the longitudinal fibers were responsible for the flexion and that the removal of the longitudinal fibers only, without removing the deep extensions of the fascia, might be sufficient for cure.

REFERENCES

Bardeen, C. R.: The Musculature in Morris' Human Anatomy, Philadelphia, 1933, P. Blakiston's Son & Co., p. 453.

Delorme: Traité d'anatomie topographique par L. Testut et O. Jacob, Paris, 1922, Gaston Doin & Cie., pp. 831, 832.

Ferrarini, M.: Morfogenesi dell' aponevrosi palmare, Pathologica **27**: 586, 1935.

Frazer, J. E.: The Anatomy of the Human Skeleton, London, 1933, J. & A. Churchill, Ltd., p. 115.

Grapow, M.: Arch. f. Anat. and Physiol. **2-3**: 1887.

Jones, F. Wood: The Principles of Anatomy as Seen in the Hand, London, 1920, J. & A. Churchill, Ltd., p. 122.

Kalberg, W.: Zur Anatomie der Palmaraponeurose, Anat. Anz. **81**: 149, 1935.

Kanavel, A., Koch, S., and Mason, M.: Dupuytren's Contraction, Surg., Gynec. & Obst. **48**: 145, 1929.

Koch, S. L.: Dupuytren's Contraction, J. A. M. A. **100**: 878, 1933.

LeDouble, A. F.: Traité des variations du système musculaire de l'homme, Paris, 1879, Schleicher Frères, Vol. II, p. 91.

Legueu, F., and Juvara, E.: Bull. Soc. Anat. de Par. 383, 1892.

Lewis, W. H.: The Development of the Muscular System in Manual of Human Embryology, by F. Kiebel and F. Mall, Philadelphia, 1910, J. B. Lippincott Company. p. 492.

Meyerding, H. W.: Dupuytren's Contracture, Arch. Surg. **32**: 320, 1936.

Poirier, P. J., and Charpy: Traité d'anatomie humaine, Paris, 1912, Masson & Cie.

Rouviere, H.: Anatomie humaine, Paris, 1927, Masson et Cie, Vol. II, p. 133.

MIXED TUMOR OF THE PAROTID GLAND WITH METASTASIS

A Case Report

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IN SPITE of many interesting and ingenious theories devised to explain the origin and nature of the mixed tumor of the salivary glands, we still must consider them as being among those tumors most apt to behave in an unexplained and unexpected manner. Few subjects in the field of oncology have aroused more controversy, and at the same time have remained so obscure in regard to the fundamental facts of their natural history. Ewing[1] has written that no single source of the mixed tumors meets all the requirements, and it is equally true that there are no criteria which will enable us safely to predict for them a benign course, local recurrence, or distant metastases. Some observers have felt that certain histopathologic characteristics were sufficient to differentiate between the clinically benign and clinically malignant growths, but, after a careful study of three hundred cases, McFarland[2] expressed the opinion that their histopathologic appearance could not be correlated with their clinical behavior. Satisfactory evidence supports his viewpoint.

These seemingly innocent tumors are notorious for their tendency to recur after local excision, and, according to Neill,[3] the incidence of recurrence in the parotid group was, until twenty years ago, sometimes as high as 75 per cent. It is encouraging to note that in more modern reports this figure is considerably lower. In Kennon's[4] series it was 15.5 per cent, and in Benedict and Meigs'[5] cases 30 per cent recurred locally after operative removal. McFarland, whose large series certainly must be a satisfactory sample upon which to base statistical studies, reported local recurrence in 23 per cent of his patients. The constantly high incidence of this unfortunate phenomenon has made the surgical treatment of these lesions unsatisfactory. At present, however, other therapeutic measures give results that are even more unsatisfactory.

In contrast to recurrence, it is quite generally agreed that metastasis is a rare event in the natural history of mixed tumors. Porter and Churchill[6] found in the literature eight cases of mixed tumors of the parotid with well-authenticated metastases. In six of these the spread was through the blood stream (Budde, Chiari, Foerster, LeClerc, LeDentu, and Payne), while in the remaining two instances (Brandes and

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Wood) the secondary deposits were in the cervical lymph glands. The case observed by Griffini and Trombetta (cited by McFarland[7]) had metastatic lesions in the bones. In addition to these cases many others are mentioned by McFarland in his review of the literature. Those least objectionable from the standpoint of correct diagnosis are the following: Two cases with cervical lymph gland metastases reported by Nasse; Partsch's case of "cylindroma" of the parotid with metastases to the pleura; a similar case with cranial metastases reported by Rispal and Samiac; and another patient who had multiple metastatic lesions of the skin, observed by Forgue, Morgue-Molmes, and Villa. A patient with a degenerated mixed tumor of the parotid upon whom Kammerer[8] operated died three and one-half years after operation with liver deposits. Olson[9] found described in the literature four cases of mixed tumor in which secondary growths were proved to be present in the lungs, and to these he added three similar cases of his own. In two of Olson's cases aberrant salivary gland tissue was the source of the tumor and in the third the original lesion was in a salivary gland and metastasized to the sternum as well as the lung. Fitzwilliams'[10] patient had metastases in the deep cervical glands, lungs, and pleura. Other cases have been reported in which the nature of the primary tumor is in doubt and it is not improbable that in some of the above cited cases the same criticism may be justified.

Whether or not carcinomatous or sarcomatous change is always present in the primary mixed tumor before metastases may occur is a highly controversial question. McFarland believes that it is not necessary to explain the clinically malignant course of some tumors on the basis of carcinomatous or sarcomatous degeneration, but that such behavior is an inherent tendency of these growths. The statement that "malignant change, whether 'sarcomatous' or 'carcinomatous,' in mixed tumors must be rare and its occurrence difficult to prove," summarizes his opinion quite accurately. Wood,[11] however, considered the metastatic lesions in two of his cases to be purely sarcomatous; Porter and Churchill believe that the secondary lesions arising from mixed tumors of the parotid are usually of carcinomatous structure. They evidently did not consider it inconsistent to think that mixed tumors metastasize through the blood stream rather than to the regional lymph nodes.

The patient whose illness we are to report is interesting because she furnishes a good illustration of some viewpoints which have been cited above and also because of some unusual features.

CASE REPORT

On June 11, 1934, a white female patient, 47 years of age, was admitted to the Christian R. Holmes Hospital on the service of Dr. Mont R. Reid. According to her history, a tumor had been present, posterior to the angle of the right mandible, during a period of five years. At first quite small, this mass had undergone a

slow, gradual growth, which had been accelerated considerably during the year before admission. This lesion had never been productive of pain or discomfort nor had it interfered with the movements of the mandible.

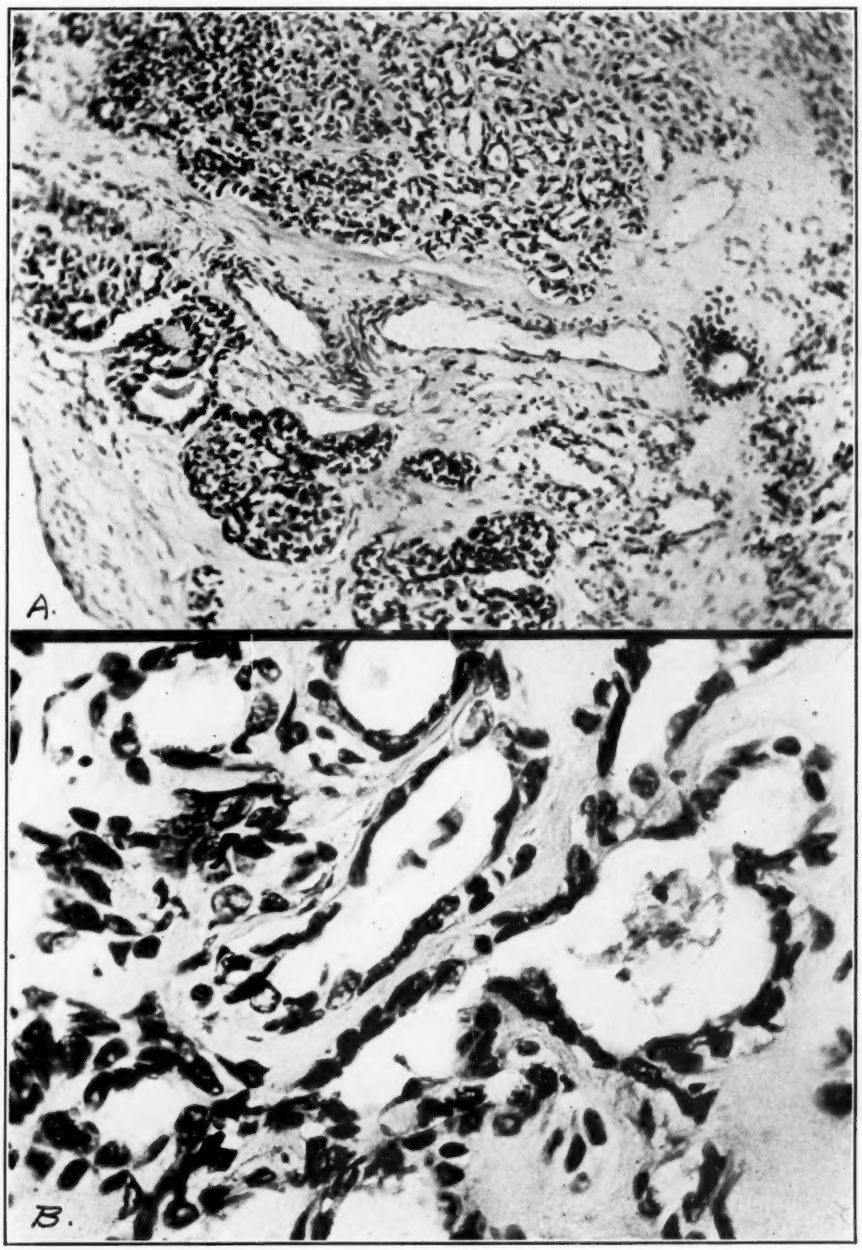

Fig. 1.—*A*, Photomicrograph (low power) of parotid tumor; *B*, photomicrograph (high power) of parotid tumor.

Examination.—In the region of the right parotid gland was a large, hard, lobulated mass whose measurements were 6 cm. by 10 cm. by 15 cm. It crowded the ear posteriorly and outward and extended down into the neck. Neither skin

attachment nor fluctuation could be demonstrated and the mass was movable on its underlying structures. The general physical examination did not reveal any pathology of importance. A clinical diagnosis of mixed tumor of the parotid gland was made without reservation.

On the day after admission, the patient was operated upon under local anesthesia. The incision was made from just below the zygomatic arch to below the angle of

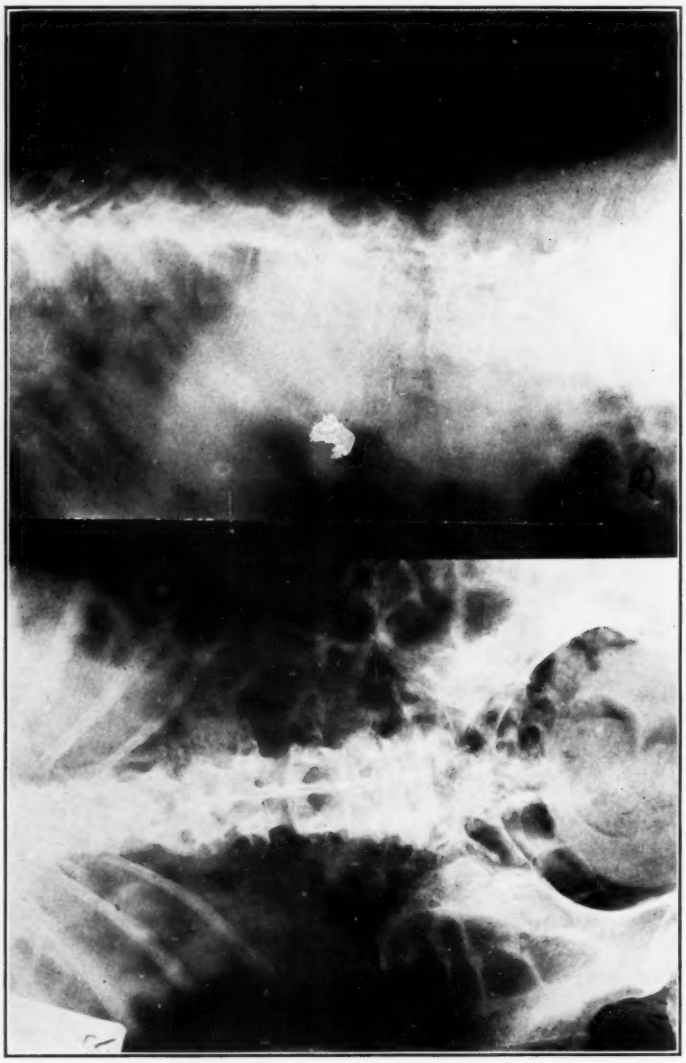

Fig. 2.—*A*, Anteroposterior view showing destructive lesion of second lumbar vertebra; *B*, lateral view showing destructive lesion of second lumbar vertebra.

the jaw, extending over the apex of the tumor. When the tumor was exposed, it proved to be a hard, encapsulated, nodular mass lying superficial to the facial nerve and presenting no gross evidence of malignant degeneration. In dissecting out the tumor, great care was used to remain outside the capsule, and after the excision was completed there was no evidence of injury of the tumor capsule or the facial nerve. All bleeding points were ligated with black silk and the skin was closed with the same material.

The pathologist reported that the lesion was an encapsulated mixed tumor of the parotid presenting highly cellular epithelial areas, interspersed with large areas

of hyalinized intercellular stroma. The cells were growing rather wildly, with alveolar arrangement in some places and no definite grouping in others. No mitotic figures were found. (Fig. 1.)

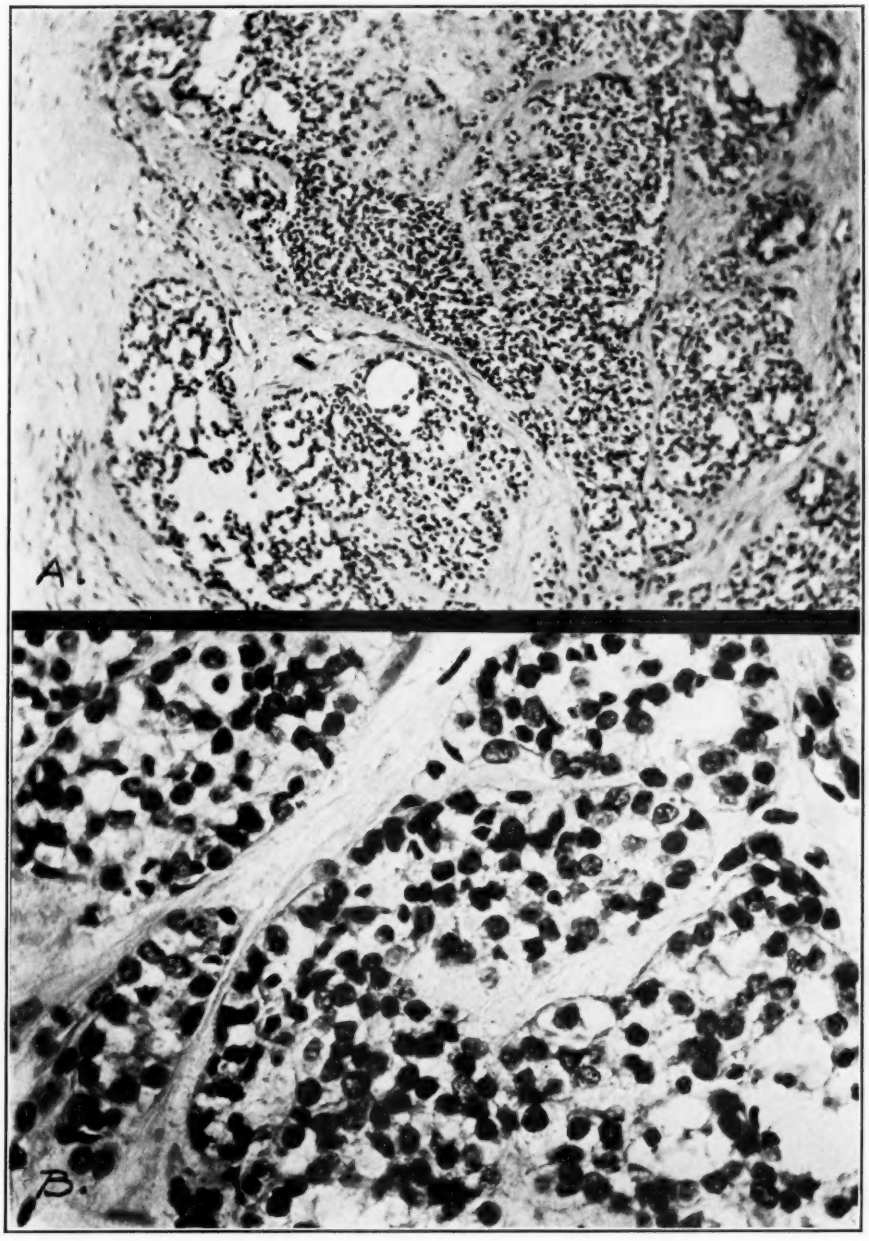

Fig. 3.—*A*, Photomicrograph (low power) of metastatic tumor of anterior abdominal wall; *B*, photomicrograph (high power) of metastatic tumor of anterior abdominal wall.

After the operation, the wound healed per primum and there was no evidence of facial nerve injury. On the third postoperative day the patient was allowed to leave the hospital.

We had no further information concerning this patient until quite recently, when a letter was received from her physician. The communication stated that her final illness had begun in December, 1936, two and one-half years after her operation. The first symptom was the development of a progressively more severe pain in the lumbar and sacral regions, and when she was examined in April, 1937, tenderness over these areas was the only significant finding. There was no evidence of local recurrence in the face or neck. Starting in the early part of September, 1937, there was severe radiation of the pain down the left leg and thigh, a symptom which was greatly aggravated by movement of the extremity. X-ray examination of the spine showed that this pain was due to a lesion which had caused almost complete destruction of the body of the second lumbar vertebra (Fig. 2). Very soon after this a subcutaneous tumor about the size of an egg was discovered on the abdominal wall below the left costal margin. This tumor had not been found at the time of the previous examination three weeks before. The lesion was surgically removed and slides made from its tissue were prepared for microscopic examination. Another lesion was discovered on Oct. 3, when a rectal examination was made because of a partial intestinal obstruction. This consisted of a hard mass felt high up in the pelvis. A few days before the death of the patient, on Oct. 18, 1937, a subcutaneous tumor was found on the left thigh.

The physician in charge of the patient was kind enough to send us one of the slides made from the metastatic growth on the anterior abdominal wall. Careful examination of the slide confirmed our belief that this lesion was the result of a metastasis from the mixed tumor of the parotid. Although its individual cells are neither as large nor as dark staining as those of the original tumor, the arrangement is similar and the same hyalinized intercellular material is present (Fig. 3). We do not believe that a diagnosis of carcinomatous or sarcomatous degeneration can be made either from the original tumor or from the metastatic lesion.

COMMENT

This case may be regarded as an exception to the rule that mixed tumors recur locally before giving rise to metastases. Of course, the period which elapsed between the date of operation and the time of death (three years, four months) is not sufficiently long to rule out the possibility of a local return of the growth, as McFarland has reported that recurrence may take place as late as forty-seven years after excision. It is entirely possible that a very small local recurrence may have escaped detection. The fact that histopathologic evidence of malignant degeneration was not apparent in either the primary or secondary growth is not unusual and agrees very well with the theories and observations of some other investigators.

SUMMARY

1. The incidence of distant metastases from a mixed tumor of a salivary gland is rare, as is shown by a brief review of the literature. In this paper such a condition occurring in a 47-year-old female patient is reported. The primary tumor was in the parotid gland.

2. The tumor did not recur locally, but three years after removing the primary lesion metastatic growths occurred in the anterior abdominal wall, the lumbar spine, pelvis, and subcutaneous tissue of the thigh.

3. Histopathologic evidence of carcinomatous or sarcomatous degeneration was present in neither the primary nor the metastatic tumor.

REFERENCES

1. Ewing, J.: Neoplastic Diseases, Philadelphia, 1938, W. B. Saunders and Co., p. 768.
2. McFarland, J.: Three Hundred Mixed Tumors of the Salivary Glands, of Which Sixty-nine Recurred, Surg., Gynec. & Obst. **63**: 457-468, 1936.
3. Neill, W., Jr.: Observations on Seventy-one Mixed Tumors of the Parotid Gland, M. J. & Rec. **136**: 187-189, 1932.
4. Kennon, R.: Tumors of the Salivary Glands, With Their After History, Brit. J. Surg. **9**: 76-86, 1921.
5. Benedict, E. B., and Meigs, J. V.: Tumors of the Parotid Gland, Surg., Gynec. & Obst. **51**: 626-647, 1930.
6. Porter, C. A., and Churchill, E. D.: Malignant Tumors of the Parotid Gland With Analysis of a Case, Surg., Gynec. & Obst. **38**: 336-343, 1924.
7. McFarland, J.: Ninety Tumors of the Parotid Region, Am. J. M. Sc. **172**: 804-848, 1926.
8. Kammerer, F.: Mixed Tumor of the Parotid Gland With Malignant Degeneration, Ann. Surg. **59**: 308-309, 1914.
9. Olson, G. W.: Pulmonary Metastases Occurring From Aberrant Mixed Salivary Gland Tumors. Report of Three Cases and Discussion, Laryngoscope **47**: 252-262, 1937.
10. Fitzwilliams, D. C. D.: Salivary Gland Tumors, Lancet **2**: 769, 1935.
11. Wood, F. C.: The Mixed Tumors of the Salivary Glands, Ann Surg. **39**: 57-97, 207-239, 1904.

LIPIODOL IN THE TREATMENT OF PERSISTENT FECAL FISTULA AFTER APPENDECTOMY

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THE treatment of fecal or postappendiceal fistula presents an interesting though perplexing problem. Operative treatment is occasionally hazardous, while conservative treatment frequently meets with stubborn failure to heal. Where the patient is a poor surgical risk, or where there is danger of contamination in surgical intervention, the only recourse is conservative treatment and the outlook often is pessimistic. For this reason, the two cases herein reported should be of interest. They suggest a new therapeutic measure, namely, introduction of lipiodol through the fistulous tract, which is worthy of further clinical trial.

CASE REPORTS

CASE 1.—K. G., a 65-year-old white housewife, was operated upon on July 6, 1934, at which time an acutely gangrenous and perforated appendix was found. The wall of the cecum was markedly involved with an acute inflammatory process. The appendix was removed and drainage was instituted. Four days following the operation the wound "broke down" and a discharge of fecal material ensued. Conservative treatment was instituted (administration of a low-residue diet and small enemas), but with no success so far as the closure of the fistula was concerned. After a stormy postoperative course, the patient was discharged on Sept. 4, 1934, with a draining fecal fistula. Before attempting to close the fistula surgically, it was decided to examine the extent, character, and course of the fistulous tract by roentgenography. For that purpose, a catheter was introduced into the fistula and lipiodol was injected. The x-ray examination revealed that "the sinus tract extends downward and inward toward the pelvis and opaque material entered the rectal pouch near its proximal portion" (Fig. 1). Immediately after this procedure, we noted a considerable diminution in the amount of fecal material exuding from the fistula and hence the operation was delayed. Complete constipation was induced by the use of tincture of opium minims three times daily, and the patient was placed on a liquid diet. Subsequently another 5 c.c. of lipiodol was injected into the tract. Within one week after the initial injection of lipiodol, the tract had closed. The patient was discharged on Nov. 27, 1934.

CASE 2.—A. G., a 55-year-old white housewife, was operated upon on Nov. 6, 1936, at which time an acute suppurative appendicitis was found and five drains were inserted. The patient had a rather stormy course with elevated temperature and was given a transfusion of 300 c.c. of blood on the eighth day postoperative. She was discharged Dec. 20, 1936, with a small amount of fecal drainage from the wound. On Feb. 4, 1937, she was again operated upon in an attempt to close the fistula. The operation was unsuccessful and the drainage continued.

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On Oct. 1, 1937, she was readmitted to the surgical service. Thorough catharsis for two days was followed by numerous cleansing enemas. After an injection of lipiodol through a catheter inserted into the fistulous tract, x-ray examination revealed "the sinus tract to extend posteriorly and medially." (Fig. 2.) "It is about 6 cm. in length and communicates with a rather large abscess cavity measuring about 4 by 3 cm."

As in the first case, immediate diminution of the fecal outflow through the tract followed the injection of lipiodol. Four further injections of from 3 to 5 c.c. of lipiodol were given at two- to three-day intervals. The fistula was completely occluded within ten days.

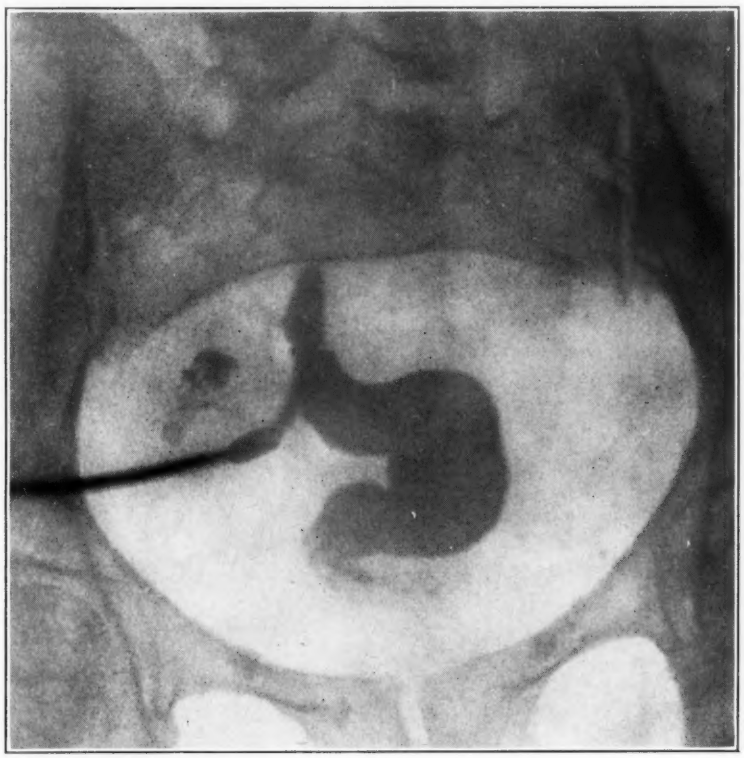

Fig. 1.—Lipiodol injection of the sinus tract in Case 1. The sinus tract extends downward and inward toward the pelvis and opaque material enters the rectal pouch near its proximal portion.

DISCUSSION

A fecal fistula consists of an outgrowth of mucous membrane from the wall of the gut which becomes continuous with the skin, thus forming a permanent canal through which a portion of the contents of the large bowel may escape. The condition is generally seen following inflammatory involvement of the wall of the cecum or ileum with necrosis and perforation. Another factor to which it has been attributed in some cases is opening of the appendiceal stump subsequent to appendectomy. This incidentally, has given rise to a controversy as to the wisdom of invaginating the appendiceal stump.

Although the literature contains numerous references to this distressing condition and emphasizes the dangers of operative interference, there are but few recent references dealing with the conservative management of these cases. Ransom and Coller, in a relatively recent report, discussed a series of ninety-four cases of fistula associated with or following appendectomy, which were treated by a variety of procedures. They conclude that operative procedure should be attempted only after failure of prolonged conservative treatment.

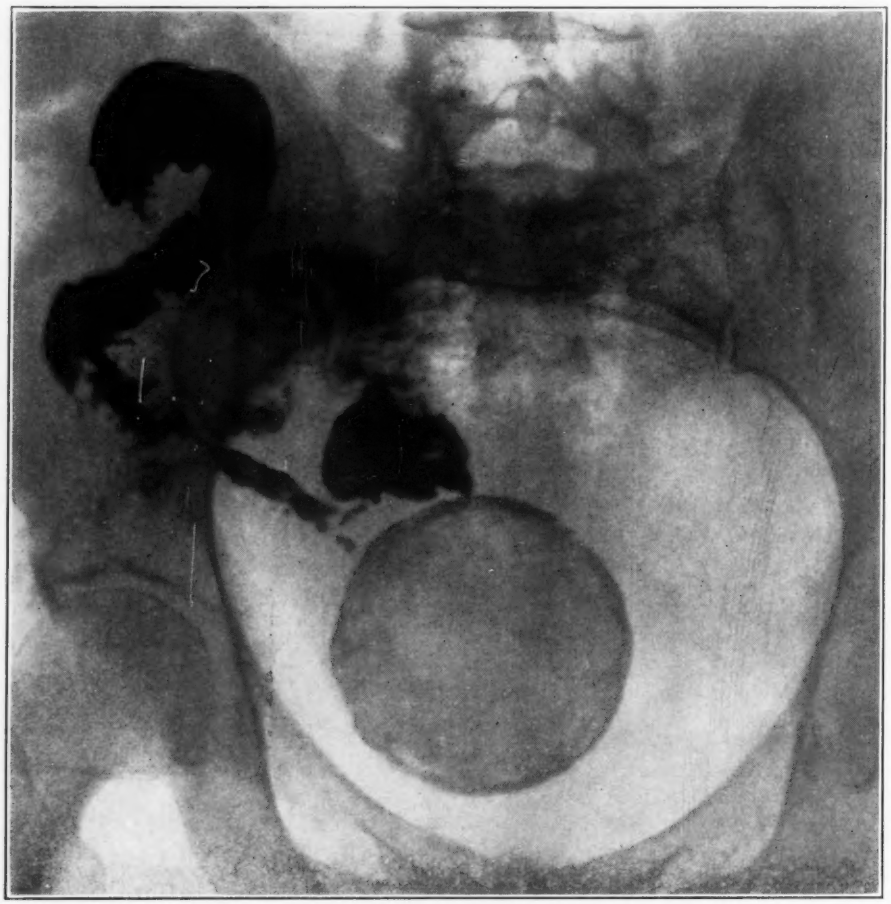

Fig. 2.—Lipiodol injection of the sinus tract in Case 2. After an injection of lipiodol through a catheter, the sinus tract is seen to extend posteriorly and medially. It is about 6 cm. in length and communicates with a rather large abscess cavity measuring about 4 by 3 cm.

It is generally agreed that the majority of fecal fistulas close spontaneously after ten to fourteen days of conservative treatment. This consists of inducing peristalsis below the site of the fistula (avoiding cathartics), giving small enemas, and feeding a low-residue diet. The outlet of the fistula is occluded either by plugging the os or by approximating its edges by pressure.

It is the remaining group, in which the fistula persists despite a long trial of the above described treatment, which constitutes the problem. The two cases presented, one of over four months' duration, and the other of almost a year, with an unsuccessful attempt at surgical intervention in the latter case, healed perfectly after several injections of lipiodol into the sinus tract. This is especially interesting in view of the observations of Ransohoff and Heiman that lipiodol is of value in the treatment of empyema cavities. While these two cases do not constitute proof of the efficacy of lipiodol in this condition, they do suggest that the procedure is worthy of further clinical trial.

We are indebted to Dr. Archie Fine and Dr. Samuel Brown for the roentgenographic studies of the patients whose cases are reported here.

REFERENCES

Ransom, H. K., and Coller, F. A.: Intestinal Fistula, J. Michigan M. Soc. **34**: 281, 1935.

Ransohoff, J. L., and Heiman, J. D.: Therapeutic Value of Lipiodol in Empyema, Surg., Gynec. & Obst. **46**: 708-710, 1928.

AN UNUSUAL COMPLICATION FOLLOWING SUBOCCIPITAL CRANIECTOMY*

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THE purpose of this communication is the presentation of an unusual complication which may follow intracranial operations upon the cerebellum.

CASE REPORT

N. S., No. 126488, a white male house painter, aged 32 years, was admitted to the Graduate Hospital on the service of Dr. J. C. Yaskin, May 4, 1936. His chief complaint was pain in the back of the neck. In May, 1935, the patient, while wrestling, sustained a sudden twist to his neck. Following this accident, he suffered from twinges of pain poorly localized in this region. By December, 1935, the discomfort in the neck was almost constant and was aggravated by motion and by straining, as in lifting heavy objects.

After thorough physical and neurological studies, the only abnormalities noted were infected ethmoid and maxillary sinuses, for which operative procedures were instituted. He was discharged from the hospital improved.

The patient was readmitted to the hospital May 5, 1937, with the same symptom of pain in the back of the neck. In addition to this complaint he developed, during the several months before admission, headache, dimness of vision, and some subjective vertigo. He evidenced some difficulty in speaking. No history of convulsions or unconscious periods was obtained.

Neurological examination on this admission disclosed lateral nystagmus, bilateral papilledema, right-sided Babinski sign, absent ankle jerks, and a spinal fluid pressure of 330 mm. of water. A space-taking intracranial lesion, presumably in the posterior fossa, was suspected and on May 20, 1937, a ventriculogram was performed. The lateral and third ventricles were symmetrically enlarged in normal position. The diagnosis of a possible cerebellar tumor was made, and on the same day the operation of suboccipital craniectomy was performed under avertin anesthesia.

The operation was attended with a great deal of difficulty because of the patient's very short, thick neck. Adequate exposure was well-nigh impossible since flexion of the head upon the chest caused respiratory embarrassment. The cerebellar tonsils were seen to enter the spinal canal and the left cerebellar lobe was larger than the right. Aside from this no other evidence of tumor was found. Bleeding was controlled by the use of silver clips. The patient made a rapid postoperative convalescence and was discharged from the hospital June 12, 1937, with practically all symptoms relieved. Before discharge he received 2,750 r. of roentgen therapy to the posterior fossa.

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On Sept. 14, 1937, he returned to the neurological clinic complaining of pain in the lateral aspect of both thighs, intensified by movement, exertion, and coughing. He had experienced fleeting pains in the thorax and abdomen since his operation, but these were not as severe as the present thigh pains. Examination at this time revealed no papilledema, bilateral nystagmus, equal but very active knee jerks, normal ankle jerks, a right-sided Babinski sign, and areas on the lateral aspects of both thighs which were hypalgesic to pinprick (Fig. 1). The hypalgesic zones corresponded to the regions in which there was a complaint of "spontaneous" pain. Roentgen examination of the dorsolumbar spine on Sept. 16, 1937, revealed two silver clips (Fig. 2), presumably in the dorsal portion of the subarachnoid space, one at the level of the first lumbar vertebra, and the other at the level of the third lumbar vertebra. He was given an analgesic to control the pain and instructed to return for readmission.

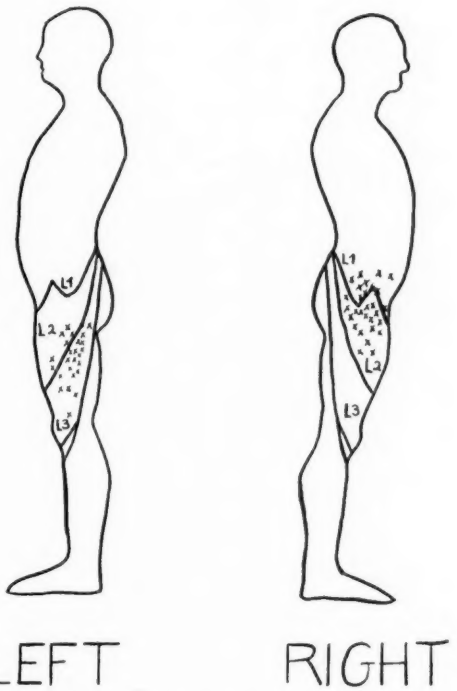

Fig. 1.—Diagrammatic representation of distribution of hypesthetic areas marked by *x* and the segmental relationship.

The patient re-entered the hospital on Oct. 11, 1937. He stated that the pain in his thighs was much relieved, but that he was generally weak and had dimness of vision and headache.

Physical examination at this time revealed lateral nystagmus and a right-sided Hoffman sign. Coincident with the diminution of the pain in the thighs, the areas of detectable hypalgesia were absent on the thighs.

Roentgen studies of the lumbar spine at this time revealed the silver clips to be in approximately the same position as in the previous study.

COMMENT

This patient demonstrates root irritation caused by silver clips which had worked themselves loose from their points of attachment and

migrated down the spinal subarachnoid space. The clips were used to control bleeding during an operation upon the cerebellum for suspected tumor.

A review of the anatomic structures of the subarachnoid space will show how such a foreign body descends from the posterior fossa to its position in the spinal canal. The arachnoid passes from the lower portion of the cerebellum to the medulla oblongata forming a triangular space beneath, called the cisterna magna. As this membrane passes down the

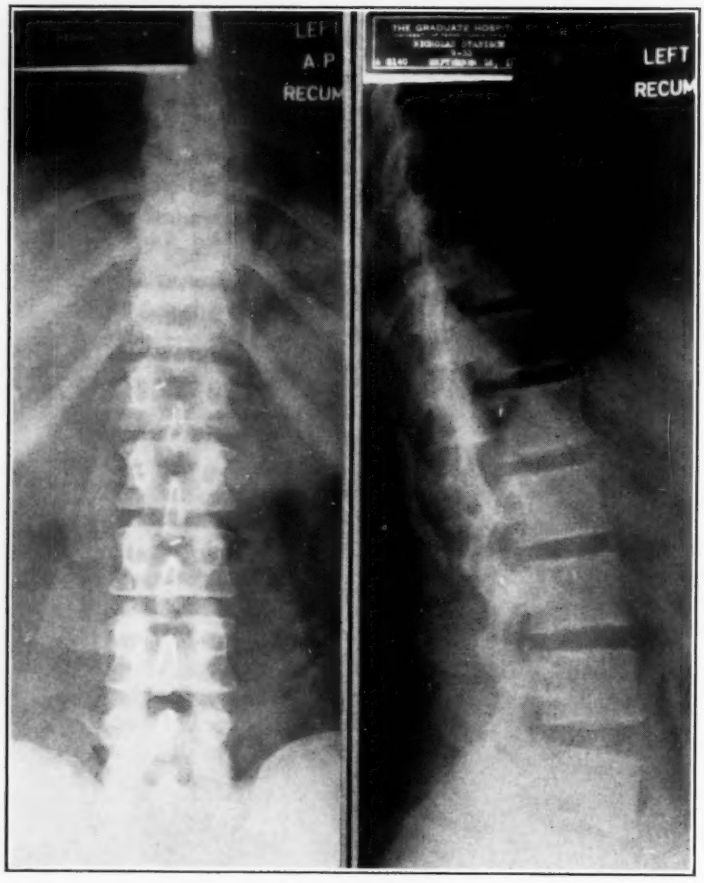

Fig. 2.—Anteroposterior and lateral roentgenograms of spine showing silver clips opposite the first and third lumbar vertebrae.

spinal canal, it is in close relationship to the dura. The space between the arachnoid and the pia mater is filled with cerebrospinal fluid. This space is divided into smaller communicating cavities by loosely formed connective tissue bands extending between the arachnoid and pia mater opposite the posterior median sulcus as well as the anterior median sulcus. Another subdivision is formed by the dentate ligament which connects the pia mater, arachnoid, and dura mater with the lateral surface of the spinal cord. The arachnoid itself follows along the spinal

nerves to a point just before the anterior and posterior roots unite outside the vertebral column. Thus a niche is formed at the exit of each root between it and the dentate ligament. At any one of these points a foreign body such as a silver clip may lodge. Furthermore, in almost every instance, the arachnoid enclosing the cisterna magna is torn during operations upon the posterior fossa so that clips which work loose have free access to the spinal subarachnoid space.

In our patient, the hypesthesia found in the areas to which pain was referred was caused by either lesions of the dorsal roots or the posterior horns of the gray matter in the spinal cord. The roentgen studies showed the lesions to be silver clips lying on the dorsal roots. The migration of silver clips in the subarachnoid space following cranial surgery is not a rare circumstance. The wonder is not that it occurs at all, but that it does not occur more often. The unusual features of this case are the extent of the migration, which is greater than has previously been noted with but one exception, in a patient in which there were no symptoms of root irritation. The second unusual feature is the fact that the silver clips caused symptoms of dorsal root irritation.

We presume that the fleeting pains in the thorax and abdomen, which occurred before the pains in the thighs, were caused by irritation of the posterior roots as the silver clips passed down the subarachnoid space. Likewise, the pain in the thighs was thought to be due to root irritation of the respective lumbar dorsal roots.

Editorial

Surgical Bacteriology

THE progress of surgery in the last fifty years has been made possible by the development of the science of bacteriology. The surgical approach to any part of the body is always made with the risk of introducing organisms which may gain a foothold, producing an infection with a more or less extensive destruction of tissue which may lead to the death of the patient.

In any general surgical service one-quarter to one-third of the cases may be classified as surgical infections, and in the office practice of any surgeon the proportion of infections is even greater. These statements make it almost self-evident that a surgeon, in order to practice his specialty with intelligence and success, must have a comprehensive understanding of the general principles of bacteriology and particularly the laboratory and clinical behavior of those organisms which are responsible for necrotizing or pyogenic infections. Extensive clinical experience often will make it possible for the surgeon to guess correctly the nature of the causative organism in the majority of surgical infections, but just as laboratory tests in many of the medical disorders minimize the percentage of error in diagnosis, cultural studies will make more exact the diagnosis in all types of surgical infection. Methods must be available to the surgeon and members of his staff to determine with accuracy the bacterial flora in any given case. Not infrequently, there is a mixture of organisms active in the lesion, or certain organisms which are present may be susceptible to specific therapy. This is particularly true because of the recent development and success of sulfanilamide in hemolytic streptococcus infections, of zinc peroxide in anaerobic infections, and bacteriophage in staphylococcus and *B. coli* infections.

Hospitals should be equipped with laboratories and personnel with expert knowledge of bacteriologic diagnostic methods; for example, the dark-field microscope, apparatus for anaerobic as well as aerobic bacterial cultivation, and media which are necessary to reveal the higher bacteria and fungi.

Anyone who has an opportunity to go about among hospitals in general finds, however, that many surgeons have very little appreciation of the necessity for more detailed knowledge of bacteriology; or, if they have, they complain about the limitations of the service which is rendered by the hospital. Time and time again, cases come into the hospital with extensive surgical infections, some acute and some long standing, in

which no attempt is made for days or even weeks to determine the nature of the causative organism. Even when time-honored methods of treatment fail to obtain results, hit or miss, or trial and error measures of one kind or another are instituted without avail, with a prolongation of illness, and suffering, and progressive destruction of tissue, often resulting in the death of a patient from a condition which might have been specifically treated had the proper bacteriologic studies been made in the earlier stages of the treatment.

The anaerobic organisms are the ones most neglected; so much so that their ready and accurate cultivation may be considered the criterion of adequate bacteriologic service. Many hospitals do not realize that anaerobic studies of the bacterial flora are always indicated in serious street accidents where the skin is broken, especially in compound fractures, likewise in all infections due to the bites of human beings or animals. All the way along the respiratory and alimentary tracts, the anaerobic organisms play an important role; in ulcerative lesions of the mouth extending directly into the tissues of the neck, or into the lymph glands; following injuries to or operative procedures upon the esophagus; after perforations of the gastrointestinal tract, especially of the lower ileum, appendix, and large bowel, resulting in general peritonitis or peritoneal abscesses; as well as in infections about the rectum and anus. These are all lesions in which the anaerobic organisms thrive. In lung abscess, bronchiectasis, and empyema the anaerobes must be kept in mind. Similarly, all gangrenous processes of the skin, particularly of the extremities, due either to the primary introduction of gangrene-producing organisms or to the interference with blood supply with secondary contamination, are fertile fields for the development of these bacteria. It is obvious, therefore, that in any general hospital the bacteriologic service should be called upon frequently for the determination of the presence of anaerobic as well as aerobic organisms. During the past year in one of the New York hospitals where the importance of this is understood, the anaerobic cultures from a surgical service of approximately 200 beds averaged more than two a day.

Realizing that many hospitals were failing to give their surgical staffs complete bacteriologic service, a year ago we sent a questionnaire to all the hospitals in New York City requesting information specifically with regard to their facilities for making anaerobic cultures, and we also asked the bacteriologist connected with the institution how often he was requested by members of the surgical staff to make anaerobic cultures. These blanks were sent out to 137 hospitals and replies came back from 76. One may assume that most of the others were not particularly interested in the subject and that little if any anaerobic bacteriology is done in most of them. Naturally no attempt was made to inquire into the methods in great detail, and the replies of the bacteriologists in charge are taken at their face value and judged accordingly.

Of the 76 hospitals which replied, 8 claimed to have full facilities for both aerobic and anaerobic bacteriologic analyses, and 6 others were fairly well satisfied with their setup. Replies of 37 made it obvious that very little anaerobic bacteriology was done and that they were not fully equipped for such studies. Of the other 25, 10 did virtually no anaerobic bacteriology and 15 had no bacteriologic laboratories at all. In answer to the question, whether the surgical department of the hospital made frequent calls upon the laboratory for anaerobic cultures, 13 of the 76 indicated that there were frequent calls for these cultures and 11 that there were occasional requests. In 34 they were made rarely and in 18, never. Yet in all of these hospitals, general surgical operations are performed almost daily.

Just where the fault lies, it is difficult to say. Usually in such matters, supply follows demand, and, if the surgeons demanded more adequate bacteriology, it would probably be forthcoming. It would seem to us, however, that the strongest demand might come from the American College of Surgeons, whose approval hospital boards of trustees hold in high esteem, and, if it were understood that fatalities in acute infections, or prolonged hospitalization with exhaustion of the economic resources of patients, were frequently the result of lack of bacteriologic facilities, the hospital management would be more interested in improving the bacteriologic service. We do not wish to minimize, however, the responsibility of the surgeons themselves. They must feel personally responsible for their cases and if they are not entirely satisfied that they have obtained all of the necessary information in connection with the etiology of their infected cases they cannot be at ease. Unquestionably a better knowledge of bacteriology or special training in this field will make the clinical surgeon better able to handle surgical infections, but any general surgeon, if he is working in a hospital where there can be a prompt and accurate determination of the causative organisms in every case, will be able to institute more promptly and intelligently the proper treatment and thus conserve the life, the limb, and the financial resources of these patients who represent such a large proportion of his practice.

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Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

SALT BALANCE IN SURGICAL PATIENTS*

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ONE of the important and commonly encountered problems in the management of surgical patients is the maintenance of a proper salt balance. Recent advances in gastrointestinal surgery and parenteral fluid administration have added to the long-standing biochemical problems created by vomiting and diarrhea so that the present-day surgeon must have a fundamental understanding of the electrolyte metabolism of the body if he is to care for his patients adequately. It is the purpose of this paper to discuss the practical aspects of sodium chloride metabolism as it relates to surgical problems and to establish simple principles for the maintenance of a proper salt balance in surgical patients.

CLARIFICATION OF TERMS

One of the most helpful laboratory aids in establishing the electrolyte status of an individual is a determination of the concentration of the chlorides in the blood plasma. This is a relatively simple and accurate procedure which can be carried out in a few minutes. It is customary in clinical practice to express chloride determinations in terms of sodium chloride.‡ This custom is not scientifically sound, because the sodium content of the plasma is more than equivalent to the chloride content, but it has the great practical advantage of expressing values in terms that are readily understood by the clinician and that can be directly applied in therapy. Thus, most physicians would immediately be confused if it were suggested that a patient be given 400 meq. of chlorine, but everyone would immediately understand if the suggestion called for 23.4 gm. of sodium chloride. Nevertheless, it is important to appreciate that chloride values expressed as sodium chloride are in no way based on sodium determinations. This applies not only to blood plasma chlorides, but also to chloride determinations on urine, vomitus, gastroduodenal, biliary, and intestinal drainage, and feces.

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‡Based on atomic and molecular weights, sodium chloride values are 1.65 times the chloride determinations.

Present methods for determining the sodium concentration in body fluids are not clinically practical. They are laborious and so time-consuming that the clinician cannot afford to wait for these determinations before formulating a program of therapy. Some indication of the sodium concentration of the plasma can be obtained from a measurement of the plasma carbon dioxide combining power. This determination indicates the amount of fixed base in excess of strong acid, or, for all practical purposes, the amount of sodium which is not balanced by chloride ions. Thus, if the body retains sodium in excess of chloride, the plasma carbon dioxide combining power will be high and a condition of alkalosis will result. On the other hand, if sodium is retained to a lesser extent than chloride, the carbon dioxide combining power will be low and inorganic acidosis will be present. Nevertheless, it must be realized that the carbon dioxide combining power is an index only of the relative concentrations of the sodium and chloride ions, and even in alkalosis a significant amount of the body sodium may have been lost. As will be pointed out later, correction of altered chloride concentration with sodium chloride will almost invariably also correct sodium deficiency and acid-base imbalance, and hence concern over correction of alkalosis or inorganic acidosis should almost always be secondary to correction of chloride depletion.

In this paper, for the practical reasons already mentioned, chloride values will be expressed in terms of sodium chloride, and for convenience the term "salt" will be used synonymously with sodium chloride.

METABOLISM OF SODIUM CHLORIDE

In order to appreciate fully the problems frequently encountered by the surgeon in sodium chloride administration, a brief discussion of salt metabolism is necessary.

Functions of Sodium Chloride.—Sodium chloride, the most abundant electrolyte in the body fluids, serves two vital functions. In the first place, it helps to maintain the acid-base balance of the body. One has only to note the variations in composition of different body fluids (Fig. 1)[1] to appreciate the intricacies involved in the maintenance of this balance and the important parts played by the sodium and chloride ions in the body chemistry. Secondly, sodium chloride, through its influence on osmotic pressure, helps to regulate the amount and distribution of body water. The total amount of water that the body can retain and the distribution of that water depends largely upon the total electrolyte composition of the body fluids. Gamble and Ross[2] have pointed out that when the chloride ion is lost from the body it is readily replaced by the bicarbonate ion which is formed from carbon dioxide. Thus, the total electrolyte content of the body remains the same and there is no significant change in the amount of body water. However,

when sodium is lost, no other ion can adequately take its place, and, in order to maintain the acid-base balance of the body, bicarbonate and chloride ions are excreted. Thus, there is a definite depletion of the total electrolyte content of the body, which in turn leads to a decrease in the total body water. This indicates that the loss of sodium ions is the essential factor in the dehydration so commonly associated with loss of gastrointestinal secretions. From these brief considerations the importance of sodium chloride in the body is apparent.

Distribution and Concentration of Sodium Chloride.—Sodium chloride is widely and fairly uniformly distributed throughout the extracellular body fluids. About 25 per cent of the body sodium is fixed in the skeleton,[3] whereas, most studies indicate that all of the chlorine exists in

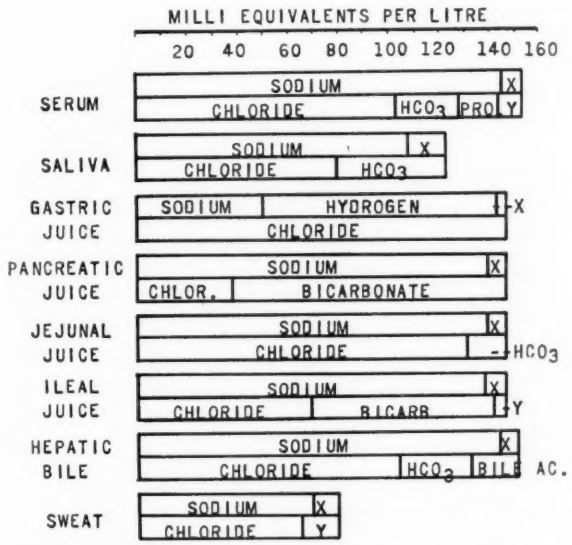

Fig. 1.—Composition of body fluids (after McCance[1]). *X*, Un-named basic radicals; *Y*, un-named acidic radicals.

ionic form.[4-7] Thus the great bulk of the sodium chloride is dissolved in the extracellular fluids. Normally, the chloride concentration in the blood plasma ranges from 560 to 630 mg. sodium chloride per 100 c.c.[4] Lymph, serous fluids,[4] and cerebrospinal fluid[8] contain a slightly higher concentration of chlorides, the additional salt being necessary to counterbalance the osmotic pressure of the proteins in the blood plasma.

Total Salt Content of the Body.—The total salt content of the human body has been estimated in various ways by a number of workers. These estimates are tabulated in Table I. Because the figure given by Sherman[13] has fitted in so well with the experimental work which will be presented later in this paper, we have assumed that it must be reasonably accurate and have adopted it in our calculations. Sherman states that the chlorine content of the body is 0.15 per cent of the body weight.

Expressed in terms of sodium chloride, this amounts to 0.248 per cent of the body weight, or 148.8 gm. of sodium chloride in a 60 kg. individual.

Salt Balance.—The sodium chloride content of the body is maintained at a normal level under ordinary conditions by the dietary intake and

TABLE I

TOTAL SALT CONTENT OF THE BODY

AUTHORITY	ACTUAL STATEMENT OF AUTHORITY	CALCULATED SODIUM CHLORIDE CONTENT OF 60 KG. MAN (GM.)
Magnus-Levy[9]	Chlorine = 0.1227% of body weight	121.7
Lotka[10]	Chlorine = 0.16% of body weight	158.4
White and Bridge[11]	The dog contains about 2.5 gm. of salt per kg. of body weight	150.0
Falconer and Lyall[12]	The total chloride content of the body is about 90 gm.	90.0
Sherman[13]	Chlorine = 0.15% of body weight	148.8

the efficient regulatory mechanism of the kidneys. The salt content of the diet varies with the taste of the individual, the average person ingesting about 8 to 12 gm. of sodium chloride per day. Of this about 2 per cent,[14] or 0.2 gm., is excreted normally in the feces and if sweating does not occur from 0.24 to 0.41 gm. (0.15 to 0.25 gm. of chlorine)[15] is lost through the skin. Thus, about 0.5 gm. of salt is lost through these two channels daily and the remainder of the salt intake, after being used for acid-base balance adjustments and for the maintenance of optimal body fluid volume, is excreted in the urine. If larger amounts of salt are excreted in diarrheal stools, sweat, or by vomiting, the salt content of the urine is correspondingly decreased. It is obvious that the salt intake must balance the salt output or else the body chemistry will be disturbed. In order to compensate for salt losses through the skin and feces and to facilitate acid-base adjustments and the maintenance of body fluid volume, we believe that the daily intake of salt should normally be about 5 to 10 gm.

Excessive Salt Intake.—If sodium chloride is ingested in large amounts, the body will dispose of it in one of two ways. (1) Usually the excess salt will be excreted promptly in the urine, provided that sufficient water is available for its excretion. The maximum concentration at which the kidneys can excrete salt is in a 2 per cent solution.[4] (2) In many sick patients much of the excess salt will be retained with water in the interstitial spaces in a concentration equal to that normally found in interstitial fluid and the individual may develop edema. These facts are illustrated in Tables II and III. Table II shows the metabolism of excessive amounts of salt in a 17-year-old male late in his convalescence from peritonitis. He had been on a general diet for a number of days prior to the beginning of this study and was excreting normal amounts

TABLE II

METABOLISM OF EXCESSIVE AMOUNTS OF SALT IN A 17-YEAR-OLD MALE SUBJECT*

24 HR. OF STUDY	BODY WEIGHT KG.	NACL INTAKE			NACL IN URINE GM.	PLASMA CHLORIDE MG. NACL/ 100 C.C.	PLASMA CO_2 COMBINING POWER %
		DIET GM.	RINGER'S SOL. IV. GM.	TOTAL GM.			
	50.52	--	--	--	--	545	52.0
1	50.64	3.3	28.6	31.9	21.1	548	57.1
2	50.46	2.2	0.0	2.2	9.2	543	55.2
Totals		5.5	28.6	34.1	30.3		

*Note the prompt excretion of salt in the urine and the insignificant variations in plasma chlorides in spite of the administration of large amounts of sodium chloride.

of salt in the urine. At the beginning of the study the patient was weighed and his plasma chlorides and carbon dioxide combining power were determined. He was then given a diet of known salt content and 3,200 c.c. of Ringer's solution containing 28.6 gm. of sodium chloride intravenously at the rate of 500 c.c. per hour. The next day the only salt ingested was a small amount in the diet. It will be noted that practically all of the salt given was soon excreted in the urine.

TABLE III

METABOLISM OF EXCESSIVE AMOUNTS OF SODIUM CHLORIDE IN SERIOUSLY ILL PATIENTS*

PATIENT	DAYS OF STUDY	TOTAL NACL GIVEN GM.	NACL EXCRETED IN URINE GM.	NACL RETAINED GM.	INITIAL PLASMA CHLORIDES MG. %	HIGHEST PLASMA CHLORIDES MG. %	GAIN IN WEIGHT KG.
A. W.	4	111.3	56.3	55.0	532	506	4.4
W. F.	4	101.8	65.1	36.7	480	597	0.6
P. G.	4	115.1	80.8	34.3	553	640	1.8
W. H.	2	51.5	22.6	28.9	554	604	3.1

*Note the tendency to gain in weight following the administration of large amounts of saline solution and also that the plasma chloride level does not rise above normal in spite of the large amounts of sodium chloride given.

Table III shows the metabolism of large quantities of salt in four seriously ill patients.[16] The salt was given intravenously in isotonic solution over periods of two to four days. All of the patients gained in weight, although the daily caloric intake in each instance was far below the actual energy requirements of the patients. This gain in weight was due to the retention of salt and water, resulting in the formation of subclinical edema.

The data in Tables II and III also illustrate another practical point about the metabolism of excessive amounts of salt. In Table II it is noted that the plasma chloride level did not change significantly in spite of the large salt intake. In Table III it will be seen that the plasma chloride level rose above the upper limits of normal in only one instance (P. G.); whereas, in Patient A. W. it actually decreased in spite of the excessive salt intake. In sickness, for reasons not yet wholly understood, the plasma chloride level often drops and frequently cannot be

raised above the lower limits of normal. In some cases even such a level cannot be maintained. This is also well illustrated by the data presented in Table IV. This patient was in poor condition two days after a partial

TABLE IV

METABOLISM OF EXCESSIVE AMOUNTS OF SALT IN A SERIOUSLY ILL PATIENT*

24 HOURS ENDING	BODY WEIGHT KG.	NACL GIVEN GM.	NACL LOST			NACL RETAINED GM.	PLASMA CHLORIDES MG. NACL/100 C.C.
			GASTROINTESTINAL TRACT DRAINAGE GM.	URINE GM.	TOTAL GM.		
4/20/38	--	--	--	--	--	--	352
4/21/38	45.30	61.5	4.8	10.9	15.7	+45.8	510
4/22/38	43.74	0	3.7	12.5	16.2	+29.6	492
4/23/38	44.06	35.5	4.8	14.3	19.1	+46.0	512

*Note that the plasma chlorides in this sick patient fail to reach the lower limits of normal in spite of the excessive administration of sodium chloride.

gastrectomy for carcinoma of the stomach, and his plasma chlorides were found to be 352 mg. sodium chloride per cent. He was given 61.5 gm. of sodium chloride intravenously in the form of physiologic salt solution. As will be shown later, this in his case is far more than sufficient salt to raise the plasma chlorides to 560 mg. per cent, yet his plasma chlorides rose only to 510 mg. per cent. Two days later he was again given an excessive amount of salt, but his plasma chlorides failed to rise above 512 mg. per cent. Thus, this sick individual was unable to attain a normal plasma chloride level in spite of excessive salt administration. These observations have an important clinical application in that they show clearly that the plasma chloride level cannot be used as an index of excessive salt administration. DeWesselow[17] made the same observation a number of years ago stating: "Balance experiments have demonstrated that chloride retention involves water retention, and that approximately a litre of water is retained for every 6 to 7 grams of sodium chloride that accumulate in the body, a normal concentration of about 0.6 per cent of sodium chloride being thus preserved in the body fluids and plasma. The result of salt retention is therefore hydraemia, rather than hyperchloraemia."

Although healthy animals will tolerate tremendous amounts of physiologic saline solution,[18, 19] the grave dangers of excessive salt administration to sick patients have been recognized by a number of workers.[17, 20-24] Not only is there danger of death from pulmonary edema, but edema may also be responsible for delayed healing of wounds. Thus, for the welfare of the patient, it is important that excessive amounts of sodium chloride should not be given.

Deficient Salt Intake.—If the intake of sodium chloride is suddenly stopped, significant amounts of salt will continue to be excreted in the

urine for several days. Benedict[25] followed the urinary excretion of chlorine in a subject fasting for thirty-one days. During this period, 20.3 gm. of sodium chloride (12.3 gm. of chlorine) were excreted in the urine. However, half of this amount was lost during the first four days. We studied four healthy individuals in this regard and found that they excreted from 3.0 to 16.7 gm. of salt in the urine during the first four days they were on a salt-poor diet. Throughout this period there was no significant alteration in the plasma chloride concentration (see Table VI and Fig. 2). It was suggested by Benedict that most of this initial salt lost was withdrawn from the skin. Because of the marked solubility of sodium chloride and because of the relatively small

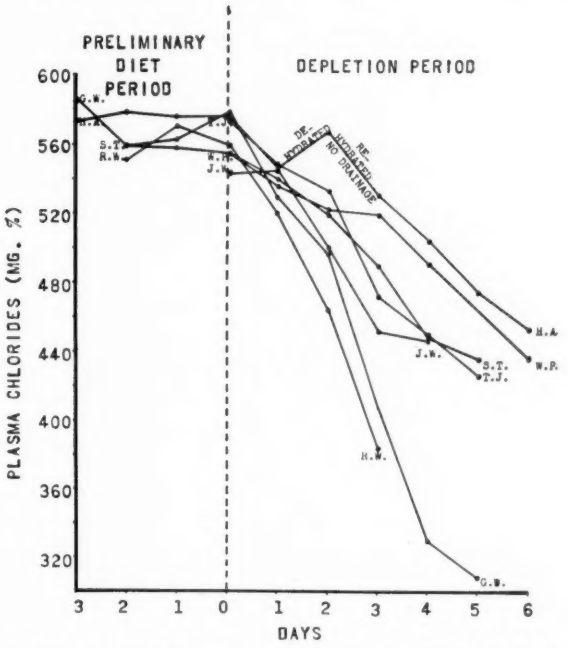

Fig. 2.—Production of hypochloremia in humans by withdrawal of gastrointestinal secretions.

amount of chloride lost in the urine during prolonged fasting, it is very doubtful that an excess of salt is stored in the body.[25, 26]

After a few days of deficient salt intake, the kidneys show remarkable ability in conserving the salt remaining in the body, the urinary excretion falling to much less than 0.5 gm. per day. If, in addition, the body loses salt by some abnormal route and the plasma chlorides fall below normal, the salt content of the urine almost invariably becomes less than 100 mg. per day. This protection of the electrolyte content of the body by the kidneys has been observed by many workers.[11, 27, 28]

Abnormal Salt Losses.—Salt may be lost from the body in considerable quantities through various channels including (1) the upper gastrointestinal tract, (2) the lower gastrointestinal tract, (3) the skin, and (4) drainage from wounds.

Salt may be lost from the upper gastrointestinal tract in vomitus, gastroduodenal drainage, or the drainage from duodenal, pancreatic, biliary, or intestinal fistulas. The salt content of these secretions as they are encountered clinically is indicated in Table V. It will be noted

TABLE V

WAYS IN WHICH SALT MAY BE LOST FROM THE BODY

SECRETION	RANGE OF NACL CONCENTRATION GM./L.	AVERAGE NACL CONCENTRATION GM./L.	SOURCES OF INFORMATION
Vomitus	1.2-6.2	3.3	Dick, Coller, and Maddock[29]
Gastroduodenal drainage (Wangensteen suction)	1.9-7.9	5.7	Analysis of 100 24-hour undiluted specimens
Hepatic bile	3.5-6.4	5.1	Analysis of 30 24-hour specimens
Intestinal fistulous drainage	3.1-6.6		Analysis of 2 specimens:
	4.7-7.9	5.2	Welch et al.[14]
	3.0-8.8		Karr and Abbott[30]
Diarrheal stools	3.7-5.2	4.3	Analysis of 3 specimens
Sweat	3.4-7.8		Camerer[35]
	1.2-4.6	4.7	Dill, et al. [36]
	4.3-8.3		Talbert and Haugen[37]
	1.2-3.3		Moss[38]

that the salt content of gastroduodenal drainage is considerably higher than that of vomitus. This is due to the fact that some of the specimens of vomitus examined were diluted by water that had been drunk shortly before the emesis occurred; whereas, none of the specimens of gastroduodenal drainage was thus diluted.

As mentioned previously, normal feces contain an insignificant amount of salt.[4, 14] Large amounts of sodium chloride may be lost, however, through the lower portion of the gastrointestinal tract when diarrhea or profuse rectal discharge is present. The significant salt losses in the stools of cholera patients were recognized over one hundred years ago.[31] The electrolyte losses in the diarrheal stools of infants and in patients with ulcerative colitis have also been found to be abnormally large.[32, 33]

Salt losses through the skin are very slight if perspiration is avoided,[15, 34] but when the sweat glands are called into action, either in high fever or in exertion at high temperatures or high humidities, the salt losses through the skin become very important.[35-38] McCance[39, 40] was able to produce salt deficiency in humans merely by causing them to sweat profusely. Various determinations of the salt concentration of sweat have been made, the more outstanding ones being summarized in Table V.

No accurate figures are available for the salt content of the exudates from wounds, but it is reasonable to assume that these will also contain significant amounts of sodium chloride. Undoubtedly, accompanying the massive exudation of large burned surfaces, there must be a considerable loss of body electrolytes.[41, 42]

In summary, it will be noted that the salt concentration of these various secretions the loss of which will lead to depletion of the body chlorides is in general about the same as the salt concentration of blood plasma; that is, about 5 to 6 gm. per liter. It is worthwhile emphasizing at this point that salt is always lost abnormally from the body in the form of an isotonic or hypotonic fluid, and therefore when replacing this salt sufficient water must also be given to make it at least isotonic. The body never loses salt without water, and water must be available to the body if it is to retain the salt that it needs.

CLINICAL ASPECTS OF LOSS OF BODY CHLORIDES—HYPOCHLOREMIA

Modes of Depletion.—Any condition associated with the loss of one or more of the previously mentioned secretions will lead to the depletion of the body chlorides with its resulting dangers. Among such conditions may be listed: pyloric and intestinal obstruction, acute poisoning, peritonitis, paralytic ileus, hyperemesis gravidarum, and postanesthetic nausea, all of these leading to vomiting or to the use of gastroduodenal suction; choledochostomy; enterostomy and fecal fistulas; ulcerative colitis, amoebic and bacillary dysentery, neoplasm of the large bowel and rectum, and similar diseases in which diarrhea is a prominent feature; and high fever and other conditions in which sweating is profuse. These conditions are so commonly encountered by the surgeon, and often by the internist and pediatrician, that it is obvious that he must frequently deal with the problem of chloride replacement.

Summary of Literature.—A tremendous amount of work has been done in recent years to establish the following significant facts: (1) Salt may be lost from the body, as already indicated, in the form of upper gastrointestinal secretions, diarrhea, sweat, and wound drainage.[2, 11, 17, 27-45, 48, 49, 51, 52, 54-57, 59, 66, 84, 86-88, 90-92, 94-96, 98-100] (2) Loss of salt in such ways results in lowering of the plasma chlorides, often in disturbances of acid-base balance, and frequently in elevation of the blood nonprotein nitrogen (azotemia).[2, 11, 17, 27, 28, 33, 40-43,45-48, 50, 52-62, 64, 68-81, 84, 88, 89, 91, 93-101] (3) Lowering of the plasma chlorides is accompanied by a fall in the salt concentration in the other body fluids and tissues.[11, 27, 28, 49, 74, 81] (4) Depletion of the body salt in itself results in definite morbidity and often in death.[2, 11, 27, 28, 31, 39, 40, 43, 45, 48, 50, 52, 54, 56, 57, 59, 81, 86, 88, 96, 99, 100] (5) The administration of saline solution is often a life-saving measure under such circumstances.[11, 28, 31, 42-45, 49, 53-56, 58, 59, 61, 63, 66, 67, 71-73, 75-77, 79-83, 85-88, 90-92, 94, 97, 99, 100] (6) The administration of electrolytes other than sodium chloride is not effective.[2, 45, 65, 71, 85]

TABLE VI

PRODUCTION OF HYPOCHLOREMIA IN HUMANS BY WITHDRAWAL OF GASTROINTESTINAL SECRETIONS

PATIENT	24 HR. ENDING	BODY WEIGHT KG.	FLUID INTAKE (5% GLUCOSE IN DISTILLED WATER I. V.) C.C.	FLUID OUTPUT			CHLORIDE LOSSES (AS NACL)			PLASMA CHLORIDES MG. NACL/ 100 C.C.	PLASMA CO_2 COMBINING POWER VOL. %
				URINE C.C.	GASTRO-INTESTINAL TRACT DRAINAGE C.C.	TOTAL C.C.	URINE GM.	GASTRO-INTESTINAL TRACT DRAINAGE GM.	TOTAL GM.		
R. W.	*11/28/37	56.60	----	2,665	----	----	2.025	----	2.025	551	43.7
	*11/29/37	57.13	----	940	----	----	0.636	----	0.636	571	46.8
	*11/30/37	56.95	----	2,390	----	----	0.359	----	0.359	559	47.1
			Total				3.020		3.020		
	12/ 1/37	53.15	2,290	2,260	3,015	5,275	0.497	12.995	13.492	520	52.7
	12/ 2/37	53.070	4,470	1,240	2,680	3,920	0.074	10.800	10.874	464	71.2
	12/ 3/37	52.240	4,280	840	1,980	2,820	0.151	10.118	10.269	384	75.1
			Total 11,040	4,340	7,675	12,015	3.742	33.913	37.655		
S. T.	*12/11/37	72.43	----	1,330	----	----	0.878	----	0.878	559	51.6
	*12/12/37	72.42	----	990	----	----	1.030	----	1.030	558	55.3
	*12/13/37	72.58	----	1,295	----	----	0.544	----	0.544	556	58.6
			Total				2.452		2.452		
	12/14/37	68.345	4,720	2,845	2,270	5,115	0.256	7.241	7.497	540	59.0
	12/15/37	67.35	4,550	2,080	1,620	3,700	0.125	7.857	7.982	520	59.2
	12/16/37	66.06	4,800	1,390	2,100	3,490	0.139	6.383	6.522	490	58.6
	12/17/37	65.92	4,860	1,505	1,700	3,205	0.090	6.324	6.414	449	63.2
	12/18/37	65.56	4,730	2,170	1,055	3,225	0.152	4.188	4.340	436	67.3
			Total 23,660	9,990	8,745	18,735	3.214	31.993	35.207		
G. W.	*1/ 4/38	75.39	----	1,815	----	----	4.990	----	4.990	586	----
	*1/ 5/38	74.61	----	1,990	----	----	1.811	----	1.811	559	----
	*1/ 6/38	72.75	----	1,620	----	----	0.842	----	0.842	563	----
	*1/ 7/38	71.53	----	1,860	----	----	0.781	----	0.781	579	51.0
			Total				8.424		8.424		
	1/ 8/38	68.84	3,201	1,810	2,760	4,570	0.561	14.794	15.255	530	----
	1/ 9/38	66.76	240	----	2,820	2,820	----	13.592	13.592	497	----
	1/10/38	67.14	4,464	355	2,175	2,530	0.046	11.006	11.052	408	----
	1/11/38	67.06	4,094	120	1,980	2,100	0.012	8.989	9.001	330	56.1
	1/12/38	----	3,414	810	0	810	0.105	0	0.105	308	53.9
			Total 15,413	3,095	9,735	12,830	9.648	48.381	58.029		

*Preliminary period on salt-poor diet of normal subject.

TABLE VI—CONT'D

H. A.	1/19/38	76.59	----	2,475	----	----	10.765	----	10.765	573	53.8
*	1/20/38	76.04	----	1,630	----	----	3.048	----	3.048	578	----
*	1/21/38	75.74	----	1,810	----	----	2.100	----	2.100	576	----
*	1/22/38	75.03	----	1,320	----	----	0.766	----	0.766	578	55.8
			Total				16.679		16.679		
	1/23/38	72.27	360	0	2,010	2,010	----	6.613	6.613	546	51.7
	1/24/38	70.01	520	822	900	1,722	0.649	3.015	3.664	568	53.1
	1/25/38	72.73	6,741	3,560	----	3,560	0.046	----	0.046	531	56.3
	1/26/38	70.05	4,612	3,005	2,310	5,315	0.270	10.511	10.781	505	49.2
	1/27/38	70.39	5,151	2,310	1,640	3,950	Nil	7.938	7.938	475	49.5
	1/28/38	70.05	4,571	1,740	1,510	3,250	0.122	6.448	6.570	454	----
		Total	15,955	11,437	8,370	19,807	17.766	34.525	52.291		
J. W.	9/13/37	59.8	----	----	----	----	----	----	----	543	51.3
	9/14/37	----	3,200	520	250	770	0.64	3.22	3.86	545	51.0
	9/15/37	----	2,780	1,180	700	1,880	0.77	3.63	4.40	500	55.4
	9/16/37	----	4,000	2,600	1,200	3,800	0.73	5.45	6.18	452	61.5
	9/17/37	58.3	4,000	2,840	710	3,550	0.28	3.38	3.66	447	61.4
		Total	13,980	7,140	2,860	10,000	2.42	15.68	18.10		
T. J.	10/ 7/37	72.7	----	----	----	----	----	----	----	574	51.0
	10/ 8/37	----	4,000	1,530	650	2,180	5.78	3.38	9.16	548	49.1
	10/ 9/37	----	4,000	3,000	1,210	4,210	1.74	8.19	9.93	533	50.7
	10/10/37	----	4,000	865	1,625	2,490	0.01	11.59	11.60	472	61.1
	10/11/37	----	4,000	1,515	150	1,665	0.05	0.10	0.14	450	61.4
	10/12/37	----	4,000	3,130	885	4,015	0.13	5.30	5.43	427	59.9
		Total	20,000	10,040	4,520	14,560	7.71	28.56	36.26		
W. P.	10/29/37	67.7	----	----	----	----	----	----	----	556	51.5
	10/30/37	----	4,500	1,330	540	1,870	2.55	2.63	5.18	536	51.5
	10/31/37	----	4,000	5,620	360	5,980	4.10	1.97	6.07	523	55.0
	11/ 1/37	----	4,000	3,740	770	4,510	2.02	3.80	5.82	520	56.7
	11/ 2/37	----	4,000	2,530	575	3,105	0.20	3.62	3.82	492	57.6
	11/ 3/37	----	4,000	2,040	600	2,640	0.16	3.74	3.90	----	----
	11/ 4/37	----	4,000	2,550	975	3,525	0.05	5.44	5.49	436	57.3
		Total	24,500	17,810	3,820	21,630	9.08	21.20	30.28		

Excellent reviews of salt metabolism with extensive bibliographies have recently been published by Kerpel-Fronius[102] and McCance.[1, 26, 40]

Experimental Hypochloremia.—In spite of these extensive investigations, however, surprisingly little quantitative work has been done in humans.[39, 40] For this reason we conducted a series of experiments on human subjects in order to correlate gastrointestinal tract losses with changes in the plasma chloride concentration. Four of the subjects (R. W., S. T., G. W., and H. A.) (Table VI and Fig. 2) were healthy individuals. The others (J. W., T. J., and W. P.) were surgical patients. The subjects were studied in the following manner. Each healthy individual was placed on a salt-poor diet and the body weight, plasma chlorides, plasma carbon dioxide combining power, and urinary chlorides were determined each day.* When the daily salt excretion in the urine became less than 1 gm., the subject was put to bed, a Levine tube was passed through the nose into the stomach, and gastrointestinal secretions were aspirated continuously by means of a Wangensteen type of suction.[106] A trap bottle was placed in the system in order to collect all of the gastrointestinal drainage. The Levine tube was irrigated regularly with air. This kept the tube open, but did not dilute the drainage as water would have done. The subject was allowed nothing by mouth except salt-free hard candy. The daily water needs were provided for by giving 5 per cent glucose in distilled water intravenously. The surgical patients were cases in which gastroduodenal suction was indicated because of their condition. They were studied in a manner similar to the normal subjects except that they were not weighed daily nor were they initially placed on a salt-poor diet, the study being started immediately after their operations. None of the subjects had stools during the period of gastroduodenal drainage. Salt losses through the skin were not determined, but in no case was there profuse sweating.

The data obtained from these studies are presented in Table VI, and the variations in the plasma chlorides are shown graphically in Fig. 2. During the period on the salt-poor diet, the plasma chloride concentration remained practically constant, but accompanying the withdrawal of chlorides in the gastrointestinal secretions the concentration of the plasma chlorides fell promptly and progressively to significantly low values. Thus, in humans as well as in animals loss of gastrointestinal secretions results in a decrease in the plasma chloride level and the figures presented in Table VI give some indication of the quantitative relationship between the total chloride lost and the resulting plasma chloride level. It is interesting to note that the concentration of salt

*In all of our studies plasma chlorides were determined by the Wilson and Ball[103] modification of the Van Slyke technique, except that the blood was not collected under oil. Determinations, however, were made promptly after the collection of specimens. Urinary chlorides and the chlorides of gastrointestinal secretions were determined by the Volhard-Arnold method,[104] the specimens being first decolorized with potassium permanganate. The carbon dioxide combining power was measured by the method described by Hawk and Bergeim[105] except that the specimens were not collected under oil.

in the gastrointestinal secretions remained fairly constant, even when the plasma chlorides were far below normal. This has also been noted by others,[99] although it has been pointed out that in the gastric secretion the amount of free acid rapidly decreases. At the conclusion of the experiments the subjects were given sufficient salt to restore the body chlorides to normal. This will be discussed later under the treatment of hypochloremia.

Restating the vast amount of work that has been done on the chemical adjustments resulting from loss of body salt, we feel that one may draw the following conclusions. The loss of body secretions containing salt results first in a fall in the plasma chlorides (hypochloremia) and in a depletion of the body chlorides in general. Soon afterward there is often an alteration in the acid-base balance and finally there is commonly a rise in the blood nonprotein nitrogen.

Chloride Loss in Excess of Sodium.—If chloride ions are lost with little loss of sodium ions, the loss of chloride ions is compensated for by an increase in bicarbonate ions. This keeps the total electrolyte composition of the body constant, and hence, if sufficient water is available, there will be little change in the total water content of the body. However, the altered proportion of sodium and chloride ions will result in alkalosis and will be indicated by a high plasma carbon dioxide combining power. If sufficient water is not available, dehydration will result; the kidneys will not have sufficient water to excrete the nitrogenous waste products, and the nonprotein nitrogen of the blood will rise. Giving water to such a patient will restore the nonprotein nitrogen to normal but will not correct the alkalosis, chloride ions being necessary for this adjustment.

Equal Loss of Chloride and Sodium.—If sodium and chloride ions are lost in equal proportions, there will be no disturbance of the acid-base balance. However, the electrolyte content of the body will be decreased and hence body water will be eliminated in an effort to keep the sodium concentration and the osmotic pressure of the body fluids constant. With this loss of body fluid, dehydration will result and nitrogenous waste products will be retained. If sodium, and with it water, continues to be lost, a certain point apparently is reached where the retention of water becomes more important to the body than the maintenance of a normal sodium concentration. In order to retain the water, we believe the body retains the nonelectrolyte urea which, being osmotically effective, leads to the partial protection of body fluid volume which has been depleted by the loss of sodium. The blood nonprotein nitrogen will rise and the administration of water in such an instance will not lower it significantly, sodium chloride being necessary as well.

Sodium Loss in Excess of Chloride.—If sodium is lost in excess of chloride ions, acidosis and a decrease in bicarbonate ions will result. There will be a loss of body fluids and an increase in the blood non-

protein nitrogen. Again water will not be effective in correcting this condition, sodium ions also being needed.

In practically all situations encountered by the surgeon, there is a loss of both sodium and chloride ions, although the relative proportion of the two may vary. In most instances where the loss is from the upper gastrointestinal tract, chlorides are lost in excess of sodium with resulting alkalosis; whereas, if the losses are from the lower intestine, sodium is lost in excess of chlorides and acidosis results. However, the treatment of alkalosis and acidosis is greatly simplified by the fact that the administration of sodium chloride and abundant amounts of water will correct either condition, the kidneys, if they are not diseased, excreting the ion that is given in excess.[107] At the same time the salt depletion of the body is corrected. Depletion of the body salt is accompanied by definite morbidity, and if the plasma chlorides fall to about half their normal value, death results.[27]

Symptoms and Signs of Hypochloremia.—The symptoms and signs resulting from depletion of the body chlorides are insidious in their onset and are often masked by the more obvious findings of the disease causing the hypochloremia. Frequently the clinician attributes certain symptoms to the disease process when in reality they are due specifically to the altered physiology resulting from the lowered body chlorides. On the basis of our observations and numerous comments in the literature,[39, 40] we have found the symptoms most constantly encountered in hypochloremia to be: (1) marked lethargy, lassitude, depression, weakness, and fatigue; (2) dulling of the sense of taste, anorexia, and nausea; (3) dulling of the mentality, drowsiness, stupor and coma; and (4) occasionally muscular twitching and cramps. The signs are less constant in their occurrence. Dehydration characterized by a dry tongue, sunken eyes, and dry, inelastic skin is often present. Alkalosis with slow shallow respirations and occasionally tetany may be encountered in cases with pyloric obstruction. Acidosis with rapid deep breathing is not uncommon in cases with severe diarrhea. A low pulse pressure has been reported in some instances. We have seen three patients with hypochloremia presenting the clinical picture of shock, and others have also noted the association of these two findings.[108] It will be noted that these are the signs and symptoms that are frequently encountered in severely ill patients from various causes, and so it is understandable why the clinician often accepts them as part of the symptom complex of the disease itself rather than attributing them to the disturbed body chemistry which is present in certain instances.

The question is frequently asked: How low must the plasma chlorides be before symptoms are produced? Because of the gradual onset and the difficulty in evaluating such early symptoms as lassitude and fatigue, a definite answer to this question can hardly be given. Some patients will show symptoms with plasma chlorides of 500 mg. per cent, and the

majority of patients if the plasma chlorides fall to 450 mg. per cent. However, more important than a knowledge of the plasma chloride level at which symptoms develop is the realization of the fact that even in patients with plasma chlorides between 560 and 500 mg. per cent there has been a definite loss of electrolytes and water from the body and this deficit ought to be corrected by the administration of saline solution if the chemical processes of the body are to be carried on most effectively.

Diagnosis of Hypochloremia.—The finding of a low plasma chloride concentration establishes the diagnosis of hypochloremia. However, this condition should always be kept in mind in any patient who is losing fluids abnormally, and it should be strongly suspected when any of the above symptoms or signs are present. Too much emphasis cannot be placed upon the importance of studying the body chemistry of patients with major surgical diseases. This is especially true of the preoperative preparation of patients. Others[77, 91, 99] have stressed the value of a rough estimation of the urinary chlorides by the simple silver nitrate precipitation test. If a low salt content of the urine is found, more extensive chemistry studies are indicated. At present we are working on an improved test for quick determination of urinary chlorides and hope that it will prove to be of value in anticipating cases of salt deficiency.

Prevention of Hypochloremia.—Hartwell and Hoguet[44] and many of the other early workers found that death from depletion of the body chlorides in experimental animals could be prevented by the administration of sufficient quantities of physiologic saline solution. Dick, Maddock, and Coller[29] have pointed out that the concentration of sodium chloride in gastrointestinal secretions is always less than the concentration of sodium chloride in physiologic saline or Ringer's solution. They have suggested that salt deficiency should not develop if one follows the rule of replacing gastrointestinal tract losses with equal volumes of physiologic saline or Ringer's solution. The same suggestion has been made by Nadler.[109]

To determine the practicability of this rule, we investigated a series of surgical patients who were losing fluids from the gastrointestinal or biliary tract, or both.* These patients were studied in the following manner: Immediately after operation each patient was weighed on a special scale; a Levine tube was passed into the stomach and continuous suction applied; and a blood specimen was taken for the determination of the plasma chlorides. The patient's water requirements were then provided for by the intravenous administration of 5 per cent glucose in distilled water. On each succeeding morning the patient was weighed, the 24-hour specimens of urine, gastrointestinal, and biliary tract drain-

*An abstract of the following experimental work was read before the American Surgical Association, Atlantic City, N. J., May 2, 1938.[110]

age (in the choledochostomy cases) were measured and their chloride content determined. A blood specimen was also taken for the determination of the plasma chloride concentration. A volume of physiologic saline or Ringer's solution equal to the volume of the drainage for the previous 24 hours was then given intravenously and this was supplemented by sufficient 5 per cent glucose in distilled water to provide for the fluid needs of the body. These patients received nothing by mouth as long as the Levine tube was in place, and none of them had stools during the period of study. Salt losses through the skin were not determined but in no case was there profuse sweating. The fluid drainage in these cases ranged from 220 to 1,960 c.c. per day. The patients did not gain in weight, so it was assumed that an excessive amount of salt leading to the development of subclinical edema had not been given.

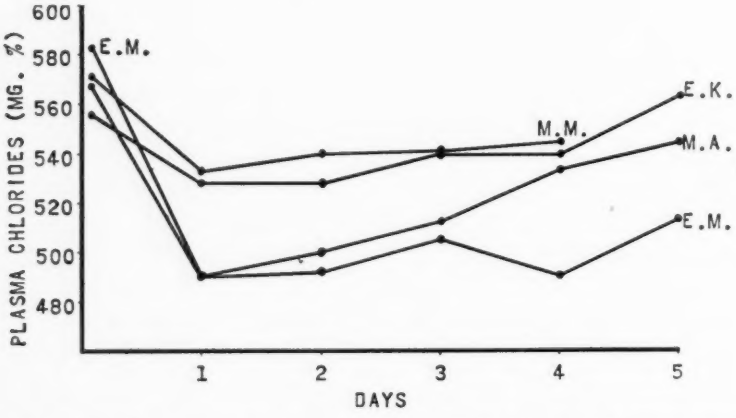

Fig. 3.—Replacement of upper gastrointestinal secretion losses with equal volumes of physiologic saline solution (1 L. equals 8.5 gm. sodium chloride).

The data presented in Fig. 3 illustrate the variations occurring in the plasma chloride level in four patients in whom losses were replaced with equal volumes of physiologic saline solution containing 8.5 gm. of sodium chloride per liter. The detailed figures of the study are given in Table VII. Three of the cases (E. K., M. M., and M. A.) maintained a fairly satisfactory plasma chloride level. Each of these cases also excreted about 1 gm. or more of sodium chloride daily in the urine, indicating, we believe at this time,* that a satisfactory excess of salt had been provided by this volume-for-volume rule. The plasma chlorides of E. M. did not fall to a seriously low level, but, nevertheless, they were definitely below normal. This may have been a failure of the volume-for-volume rule or an example of an individual whose plasma chlorides could not be maintained at a higher level.

Fig. 4 and Table VIII show a series of four cases in which the losses were replaced with equal volumes of Ringer's solution containing the

*This statement needs further investigation.

TABLE VII

REPLACEMENT OF UPPER GASTROINTESTINAL SECRETION LOSSES WITH EQUAL VOLUMES OF PHYSIOLOGIC SALINE SOLUTION

(1 L. ⇔ 8.5 GM. OF SODIUM CHLORIDE)

PATIENT	24 HR. ENDING	BODY WEIGHT KG.	FLUID OUTPUT					FLUID INTAKE				SODIUM CHLORIDE LOSSES					NACL GIVEN GM.	PLASMA CHLORIDE MG. NACL/100 C.C.
			URINE C.C.	GASTRO-INTESTINAL TRACT C.C.	BILE T-TUBE C.C.	TOTAL C.C.	TOTAL LOSSES TO BE REPLACED C.C.	5% GLUCOSE INTRAVENOUSLY C.C.	PHYSIOLOGIC SALINE C.C.	WATER (ORALLY) C.C.	TOTAL C.C.	URINE GM.	GASTRO-INTESTINAL TRACT GM.	BILE T-TUBE GM.	TOTAL GM.	TOTAL NACL TO BE REPLACED GM.		
E. K.	2/18/38	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	556
	2/19/38	49.36	1,870	320	400	2,590	720	4,000	0	0	4,000	2.45	1.03	1.91	5.39	2.94	0	528
	2/20/38	47.86	3,650	850	290	4,790	1,140	3,110	708	0	3,818	1.10	5.81	1.69	8.60	7.50	6.03	528
	2/21/38	48.26	2,470	0	290	2,760	290	3,050	1,165	0	4,215	1.06	0	1.75	2.81	1.75	9.90	540
	2/22/38	47.67	2,770	0	250	3,020	250	2,075	287	995	3,357	1.11	0	1.49	2.60	1.49	2.44	540
	2/23/38	47.44	2,170	0	250	2,420	250	1,020	478	1,500	2,998	1.26	0	1.01	2.27	1.01	4.06	564
		Total	12,930	1,170	1,480	15,580	2,650	13,255	2,638	2,495	18,388	6.98	6.84	7.85	21.67	21.67	22.43	
M. M.	2/21/38	42.01	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	571
	2/22/38	42.62	2,100	220	0	2,320	220	2,970	890*	0	3,860	6.85	0.56	0	7.41	0.56	5.86	533
	2/23/38	41.32	2,900	350	0	3,250	350	3,000	243	0	3,243	1.42	2.23	0	3.65	2.23	2.07	540
	2/24/38	41.65	2,180	390	0	2,570	390	2,730	354	0	3,084	1.11	2.45	0	3.56	2.45	3.01	541
	2/25/38	40.26	1,460	0	0	1,460	0	1,990	385	0	2,375	1.53	0	0	1.53	0	3.27	545
		Total	8,640	960	0	9,600	960	10,690	1,872	0	12,562	10.91	5.24	0	16.15	5.24	14.21	
E. M.	3/ 9/38	58.01	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	582
	3/10/38	59.06	1,040	900	0	1,940	900	4,000	0	0	4,000	1.21	6.46	0	7.67	6.46	0	490
	3/11/38	57.25	3,750	840	0	4,590	840	3,020	865	0	3,885	1.65	4.94	0	6.59	4.94	7.35	492
	3/12/38	56.85	2,620	920	0	3,540	920	3,055	835	0	3,890	1.51	5.69	0	7.20	5.69	7.01	505
	3/13/38	56.30	950	1,020	0	1,970	1,020	1,400	922	0	2,322	0.70	5.30	0	6.00	5.30	7.84	490
	3/14/38	56.50	1,250	0	0	1,250	0	1,020	1,030	650	2,700	0.80	0	0	0.80	0	8.76	513
		Total	9,610	3,680	0	13,290	3,680	12,495	3,652	650	16,797	5.87	22.39	0	28.26	22.39	30.96	
M. A.	4/ 5/38	54.46	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	568
	4/ 6/38	----	940	490	160	1,590	650	3,300	0	0	3,300	2.17	3.31	0.81	6.29	4.12	0	490
	4/ 7/38	53.26	3,540	780	240	4,560	1,020	3,000	669	0	3,669	3.12	5.37	1.03	9.52	6.40	5.69	500
	4/ 8/38	51.29	2,830	910	230	3,970	1,140	2,000	1,010	0	3,010	1.59	6.53	1.10	9.22	7.63	8.59	512
	4/ 9/38	50.87	1,880	0	215	2,095	215	2,000	1,150	0	3,150	0.98	0	1.08	2.06	1.08	9.78	535
	4/10/38	50.92	2,700	0	220	2,920	220	2,250	393	1,000	3,643	0.76	0	1.14	1.90	1.14	3.34	545
		Total	11,890	2,180	1,065	15,135	3,245	12,550	3,222	1,000	16,772	8.62	15.21	5.16	28.99	20.37	27.40	

*465 c.c. physiologic saline and 425 c.c. blood.

equivalent of 7.5 gm. of sodium chloride per liter.* It will be noted that all of the cases maintained a fairly satisfactory plasma chloride level, but in each the daily urinary excretion of salt fell below 1 gm. indicating that an insufficient excess of salt had been administered.

In all except one of the cases in Figs. 3 and 4 (W. W. in Fig. 4), there was a definite fall in the plasma chloride concentration during the first 24 hours of gastrointestinal fluid drainage, no salt being given during this period. A fairly constant level was maintained thereafter by the volume-for-volume replacement with a tendency in most cases for the level to rise on the last day. In an attempt to eliminate this initial drop and thus maintain the plasma chlorides at a more satisfactory level a series of four cases was studied in which arbitrarily about 1,000 c.c. of physiologic saline solution was given during the first 24 hours. Thereafter the losses were replaced volume-for-volume with physiologic saline solution as in the previous cases.

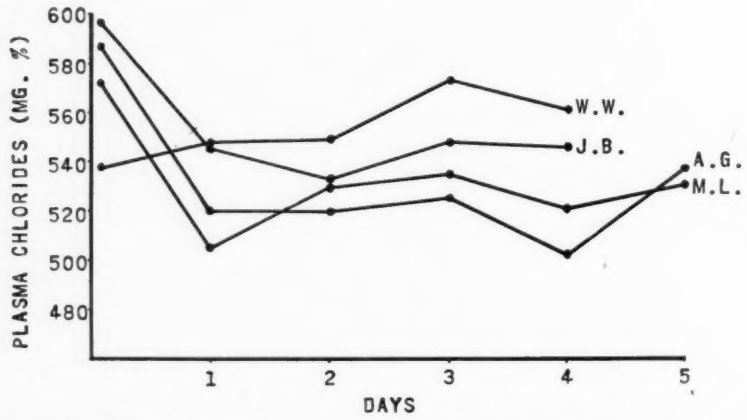

Fig. 4.—Replacement of upper gastrointestinal secretion losses with equal volumes of Ringer's solution (1 L. equals 7.55 gm. sodium chloride).

The results of this study are shown in Fig. 5 and Table IX. It will be seen that three of the cases (T. D., L. W., and M. L.) showed an initial drop in the plasma chlorides in spite of the administration during the first 24 hours of more than sufficient saline solution to balance the abnormal losses during this period. However, the fall was not as marked as in the preceding cases in which no saline solution was given during the first day, and the plasma chloride levels maintained were higher than in the previous cases. This procedure, therefore, appears to be a valuable addition to the volume-for-volume rule.

In summary, the prevention of hypochloremia depends upon the adequate replacement of abnormal losses of chlorides from the body. These studies indicate that this can be accomplished by replacing abnormal fluid losses with equal volumes of physiologic saline solution. This iso-

*Ringer's solution as made by different laboratories varies in its composition. Locke-Ringer's solution U.S.P. contains 9.6 gm. of chloride expressed as sodium chloride.

Table VIII

Replacement of Upper Gastrointestinal Secretion Losses with Equal Volumes of Ringer's Solution

(1 L. = 7.5 Gm. NaCl)

Patient	24 hr. ending	Body weight Kg.	Fluid output					Fluid intake				Sodium chloride losses						Plasma chloride mg. NaCl/100 c.c.
			Urine c.c.	Gastro-intestinal tract c.c.	Bile T-tube c.c.	Total c.c.	Total losses to be replaced c.c.	Ringer's soln. intravenously c.c.	5% glucose intravenously c.c.	Water (orally) c.c.	Total c.c.	Urine gm.	Gastro-intestinal tract gm.	Bile gm.	Total gm.	Total NaCl to be replaced gm.	NaCl given gm.	
W. W.	1/ 4/38	81.77	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	538
	1/ 5/38	80.00	680	960	1,000	2,640	1,960	0	1,750	0	1,750	0.73	4.15	5.82	10.70	9.97	0	548
	1/ 6/38	78.82	2,590	290	810	3,690	1,100	2,035	2,000	0	4,035	0.54	1.84	5.04	7.42	6.88	15.36	549
	1/ 7/38	77.81	2,410	0	315	2,725	315	1,133	2,970	0	4,103	2.10	0	2.03	4.13	2.03	8.55	573
	1/ 8/38	76.96	465	0	0	465	0	318	3,100	0	3,418	0.35	0	0	0.35	0	2.30	561
		Total	6,145	1,250	2,125	9,520	3,375	3,486	9,820	0	13,306	3.72	5.99	12.89	22.60	18.88	26.21	
J. B.	1/10/38	73.00	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	596
	1/11/38	74.50	745	480	0	1,225	480	0	4,100	0	4,100	3.86	2.65	0	6.51	2.65	0	545
	1/12/38	73.23	3,960	505	0	4,465	505	485	4,120	0	4,605	5.19	3.30	0	8.49	3.30	3.66	533
	1/13/38	72.33	2,520	280	0	2,800	280	522	3,020	0	3,542	0.48	1.57	0	2.05	1.57	3.81	548
	1/14/38	72.07	1,335	0	0	1,335	0	318	2,040	400	2,758	0.32	0	0	0.32	0	2.40	546
		Total	8,560	1,265	0	9,825	1,265	1,325	13,280	400	15,005	9.85	7.52	0	17.37	7.52	9.87	
A. G.	1/10/38	51.64	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	586
	1/11/38	----	735	320	190	1,245	510	800*	2,000	0	2,800	1.61	2.47	1.04	5.12	3.51	4.80	520
	1/12/38	49.65	3,300	775	180	4,255	955	517	4,000	0	4,517	1.02	6.07	1.11	8.20	7.18	3.90	520
	1/13/38	48.78	2,600	855	130	3,585	985	945	3,000	0	3,945	0.49	6.67	0.82	7.98	7.49	7.13	526
	1/14/38	48.25	2,260	860	70	3,190	930	963	3,000	0	3,963	0.34	5.62	0.33	6.29	5.95	7.27	502
	1/15/38	49.38	1,120	0	150	1,270	150	956	2,000	1,000	3,956	0.27	0	0.88	1.15	0.88	7.22	538
		Total	10,015	2,810	720	13,545	3,530	4,181	14,000	1,000	19,181	3.73	20.83	4.18	28.74	25.01	30.32	
M. L.	1/24/38	52.91	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	571
	1/25/38	52.15	2,180	570	290	3,040	860	0	4,000	0	4,000	4.82	4.01	1.59	10.42	5.60	0	505
	1/26/38	49.85	3,390	540	340	4,270	880	835	3,060	0	3,895	0.51	2.99	1.63	5.13	4.62	6.30	530
	1/27/38	49.03	2,890	520	250	3,660	770	900	2,975	0	3,875	0.17	3.49	0.92	4.58	4.41	6.79	535
	1/28/38	49.76	2,750	0	300	3,050	300	787	2,080	0	2,867	0.06	0	1.26	1.32	1.26	5.93	521
	1/29/38	49.06	1,870	0	260	2,130	260	317	1,030	1,100	2,447	0.13	0	1.57	1.70	1.57	2.39	531
		Total	13,080	1 630	1,440	16 150	3,070	2,839	13,145	1,100	17,084	5.69	10.49	6.97	23.15	17.46	21.41	

*300 c.c. physiologic saline and 500 c.c. blood.

TABLE IX

REPLACEMENT OF GASTROINTESTINAL SECRETION LOSSES WITH EQUAL VOLUMES OF PHYSIOLOGIC SALINE SOLUTION PLUS 1,000 C.C. OF PHYSIOLOGIC SALINE DURING THE FIRST 24 HOURS

			FLUID OUTPUT					FLUID INTAKE				SODIUM CHLORIDE LOSSES						
PATIENT	24 HR. ENDING	BODY WT. KG.	URINE C.C.	GASTROINTESTINAL TRACT C.C.	BILE T-TUBE C.C.	TOTAL C.C.	TOTAL TO BE REPLCD. C.C.	PHYSIOLOGIC SALINE INTRAVENOUS C.C.	5% GLUCOSE INTRAVENOUS C.C.	WATER ORALLY C.C.	TOTAL C.C.	URINE GM.	GASTROINTESTINAL TRACT GM.	BILE GM.	TOTAL GM.	TOTAL TO BE REPLACED GM.	NACL GIVEN GM.	PLASMA CL. MG. NACL/100 C.C.
T. D.	3/16/38	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	591
	3/17/38	66.20	1,200	120	0	1,320	120	1,050	2,700	0	3,750	3.77	0.80	0	4.57	0.80	8.91	561
	3/18/38	65.15	2,190	110	0	2,300	110	120	3,000	0	3,120	1.01	0.76	0	1.77	0.76	1.02	568
	3/19/38	63.62	2,830	335	0	3,165	335	110	3,000	0	3,110	1.33	2.27	0	3.60	2.27	0.93	578
	3/20/38	64.03	630	0	0	630	0	342	1,000	1,000	2,342	0.50	0	0	0.50	0	2.91	584
		Total	6,850	565	0	7,415	565	1,622	9,700	1,000	12,322	6.61	3.83	0	10.44	3.83	13.77	
E. R.	3/19/38	46.56	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	559
	3/20/38	47.29	560	630	0	1,190	630	1,010	2,600	0	3,610	0.36	4.50	0	4.86	4.50	8.60	663
	3/21/38	45.30	3,260	1,020	0	4,280	1,020	630	3,000	0	3,630	0.46	7.53	0	7.99	7.53	5.36	563
	3/22/38	44.11	1,160	1,890	0	3,050	1,890	1,020	2,000	0	3,020	0.13	12.36	0	12.49	12.36	8.65	553
	3/23/38	43.21	1,300	2,500	0	3,800	2,500	1,920	2,000	0	3,920	0.09	19.28	0	19.37	19.28	16.32	530
	3/24/38	43.17	360	3,000	0	3,360	3,000	2,510	1,000	240	3,750	0.14	20.76	0	20.90	20.76	21.33	528
	3/25/38	42.54	440	2,330	0	2,770	2,330	3,080	0	0	3,080	0.41	15.38	0	15.79	15.38	26.20	611
		Total	7,080	11,370	0	18,450	11,370	10,170	10,600	240	21,010	1.59	79.81	0	81.40	79.81	86.46	
L. W.	3/22/38	58.09	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	579
	3/23/38	59.22	310	320	0	630	320	1,060	2,000	0	3,060	3.08	1.96	0	5.04	1.96	9.01	543
	3/24/38	57.09	3,680	310	0	3,990	310	325	3,000	0	3,325	9.02	1.82	0	10.84	1.82	2.76	546
	3/25/38	54.45	3,230	600	0	3,830	600	314	2,000	0	2,314	1.97	4.01	0	5.98	4.01	2.67	594
	3/26/38	55.46	280	0	0	280	0	582	500	1,400	2,482	0.64	0	0	0.64	0	4.91	592
		Total	7,500	1,230	0	8,730	1,230	2,281	7,500	1,400	11,181	14.71	7.79	0	22.50	7.79	19.35	
M. L.	4/12/38	40.08	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	602
	4/13/38	40.94	1,160	260	220	1,640	480	1,606*	2,000	0	3,600	1.33	1.59	1.28	4.20	2.87	11.41	578
	4/14/38	39.08	3,230	250	390	3,870	640	486	3,000	0	3,486	4.81	1.69	2.00	8.50	3.69	4.13	568
	4/15/38	38.87	1,620	0	370	1,990	370	632	2,500	0	3,132	1.59	0	2.07	3.66	2.07	5.37	569
	4/16/38	37.64	730	0	390	1,120	390	722	1,000	800	2,522	2.12	0	2.17	4.29	2.17	6.14	558
		Total	6,740	510	1,370	8,620	1,880	3,440	8,500	800	12,740	9.85	3.28	7.52	20.65	10.80	17.05	

*1,050 c.c. physiologic saline and 550 c.c. blood.

tonic solution provides not only for the sodium and chloride losses but also for the water losses. In view of the fact that most surgical patients lose sodium dichloride during the first 24 hours after operation, it is advisable to give in addition about 1 L. of physiologic saline solution during this period to decrease the initial fall in the plasma chloride concentration which frequently occurs. If it is apparent that the patient will lose more than 1,000 c.c. of gastrointestinal or other secretions during this period, the amount of saline solution given during the first 24 hours should be increased accordingly.

This volume-for-volume replacement rule is of practical importance in the management of patients losing fluids abnormally while under the care of a physician. Such patients may be vomiting or may have diarrhea, but the rule is most useful in patients in whom continuous gastroduodenal suction is used. One precaution must be observed in such instances. Some physicians allow patients with inlying gastro-

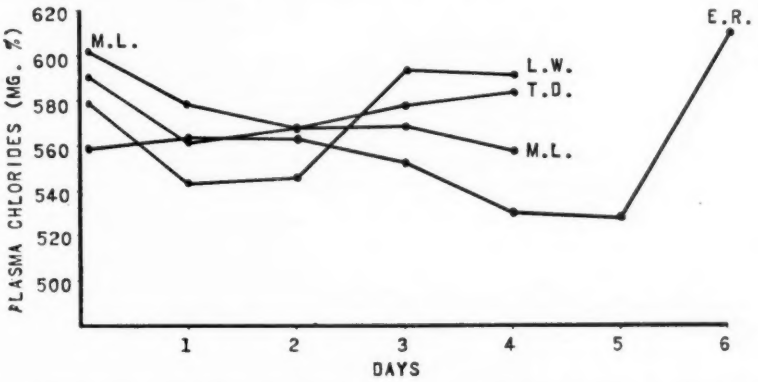

Fig. 5.—Replacement of upper gastrointestinal secretion losses with physiologic saline solution plus 1,000 c.c. of physiologic saline during the first 24 hours.

duodenal suction to take water by mouth or irrigate the tube with water. Most, but not all, of this water will be promptly aspirated, but in it will be dissolved small but significant amounts of chlorides drawn from the body. If the amount of water drunk or used for irrigation is deducted from the total drainage and the remaining portion replaced by the volume-for-volume rule, a definite deficit will be introduced and the patient will probably develop salt deficiency. On the other hand, if the total drainage including the water drunk and used for irrigation is replaced with an equal volume of physiologic saline solution, unnecessarily large quantities of salt will be given with its attendant dangers. In order to avoid such complicating factors we believe that the Levine tube should be irrigated with air rather than water and the patient should be allowed only sufficient ice chips by mouth to keep him comfortable.

(To be continued in the October issue. The references will accompany the second section.)

Review of Recent Meetings

REVIEW OF THE MEETING OF THE AMERICAN SURGICAL ASSOCIATION, ATLANTIC CITY, N. J., MAY 2-4, 1938

ALBERT O. SINGLETON, M.D., GALVESTON, TEX.

The Therapeutic Management of Urinary Infections: Alexander Randall, Philadelphia, Pa., and **Boland Hughes.**—"All urinary infections are of either hematogenous or urogenous (adnexal) origin. Rational treatment should be directed first towards eliminating the infectious focus or foci feeding the urinary tract. So far as the urinary infection per se is concerned, three cardinal principles govern the treatment. (1) Removal of all causes of urinary stasis; (2) determination of adequacy of kidney function to excrete the chosen antiseptic in sufficient concentration to obtain therapeutic effect; (3) selection of the proper antiseptic for specific action on the infecting organism."

Thymol Therapy in Actinomycosis: Thomas M. Joyce, Portland, Ore.—"Experiments with various volatile oils have demonstrated that thymol is the most efficacious in destroying certain types of yeasts. A culture of actinomycosis proved readily susceptible to an aqueous solution of thymol, but resistant to other oils. A case of cervicofacial actinomycosis, treated by the oral administration of thymol with definite improvement, was reported by Myers and Thienes in 1925. After further experimentation Myers, 1927, concluded that powdered thymol in capsules by mouth was absorbed and circulated in sufficient strength to have pronounced fungicidal effect on two patients with pulmonary moniliosis and one with actinomycosis; also he felt that localized superficial mycotic infections may be treated with solutions of the oils and thymol in alcohol, ether, or olive oil, in strength according to local irritability of the tissues."

Thymol was found (1925) to cure mycelia. It is given 5 per cent in cinnamon oil orally, ½ gr. (in capsule) daily. A 10 per cent solution in oil is injected in the sinuses daily. Six cases were reported improved or cured with the treatment.

Discussed by: **Owen H. Wangensteen,** Minneapolis, Minn., who has succeeded equally well by surgery alone. Based upon the fact that the infection is anaerobic and grows in dead tissue, curettement seems to be all that is necessary.

The Education and Training of a Surgeon (Presidential Address): **Arthur W. Elting,** Albany, N. Y.—Dr. Elting made a strong plea for activity of hospitals in this problem. Each hospital should and could provide training for the young surgeon with little added expense and improvement in the service to the patients. Surgeons as a group should sponsor such a plan. The usual extravagance of the surgeon should be directed to financing such a plan in the hospital. At the present time only forty-four hospitals in the United States give as much as three years' training to young surgeons. Dr. Elting also discussed the nursing school problem. He said "training of nurses is in the hands of women with a great crusading zeal, and though the surgeon has to use the nurse he has too little to do with her training

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program.'' He suggests a board from the A. M. A., American College of Surgeons, and other organizations to inspect and standardize hospitals upon a basis of training the young surgeon.

A National Council on Medical Education: Willard C. Rappleye, New York, N. Y., Dean of Columbia University and president-elect of the Association of American Medical Colleges.—''The educational problems of medicine from college preparation to retirement from practice, should be regarded merely as different phases of the training of personnel to meet the health needs of the country. Portions of the training are primarily within the jurisdiction of universities and medical schools, some are largely within the domain of the hospitals, others are in the various fields of practice, and some are under direct governmental regulations. There is urgent need for co-ordination of the various subdivisions of medical education and of the programs of national and state agencies, universities, hospitals and professional bodies dealing with portions of the whole program. The logical conclusion from the present unrelated and frequently overlapping efforts is to secure a national co-ordinating body representative of the major activities in medical education. A National Council on Medical Education, Licensure, and Hospitals should be created, made up of representatives of the universities, medical schools, hospitals, practicing profession, specialty boards, state licensing bodies, and public health agencies. The functions of a National Medical Council would be those of studying the major educational needs of American medicine, of formulating adequate standards of training at the several levels and of advising regulatory bodies, universities, hospitals and governmental agencies on standards, methods and procedures. A central clearing house for authoritative judgement and advice on matters dealing with all features of medical education, transcending the activities and interests of any one group or organization, would be of the greatest practical value to the future health program of the entire country.''

Discussed by **Evarts A. Graham,** St. Louis, Mo., and **Harold Rypins,** of the New York Board of Medical Examiners.

Replacement of Sodium Chloride in Surgical Patients: Frederick A. Coller, Robert M. Bartlett, Ann Arbor, Mich., **Svend Pedersen, Dermid L. C. Bingham,** and **Walter G. Maddock,** Ann Arbor, Mich.—''The problem of maintaining a satisfactory electrolyte balance in surgical patients losing gastrointestinal secretions has been frequently discussed, but the amount of salt given has been largely on an empirical basis. The dangers of overloading a patient with salt have been known for some time and the equally important dangers of depletion of body chlorides have also been recognized. Quantitative studies have been undertaken on two phases of the problem: (1) how much salt does a patient who has had prolonged vomiting or other abnormal losses of body fluids need to restore the blood chlorides to a normal level, and (2) how much salt does a patient losing his gastrointestinal secretions while under observation, as on continuous gastroduodenal suction, need to maintain his blood chlorides at a normal level. In the patient entering the hospital with depleted body chlorides, studies tend to show that if the surgeon knows the body weight of the patient and the blood chloride level he can calculate by means of a simple formula the number of grams of salt that should be administered to the patient to restore his electrolyte balance to normal. Results indicate that by replacing the drainage from Wangensteen suction volume for volume with physiological saline or Ringer's solution, the blood chlorides will be maintained at their original level and yet the body will not be overloaded with an excessive amount of salt.''

Discussion by **Thomas G. Orr,** Kansas City, Mo.—''Sodium chloride may be given in excess and do harm especially when the patient has a low proteid state, even though there would be no danger in good health.''

The Repair of Abdominal Incisions: Allen O. Whipple, New York, N. Y.—"Certain large hospitals have reported 2 per cent to 6 per cent of wound disruption, especially following operations in the upper abdomen. In an effort to repair abdominal wounds, a technique has been developed that has yielded far better results than formerly. In a series of 314 cases, chiefly upper abdominal, silk was used in 212 and catgut in 102. The same principle was carried out with both suture materials: (1) Accurate apposition of the peritoneum and posterior muscle sheath by continuous suture followed by interrupted suture. Anterior rectus sheath closed by the vertical suture, the "far-and-near stitch." Interrupted sutures used for this layer also. Skin and subcutaneous tissues sutured with interrupted silk. (2) Suture material, whether silk or chromic, much finer than usually employed, and of a strength no greater than the strength of the tissues holding the suture. Silk grade C or O catgut was used. (3) Because of the principles of the far-and-near stitch and the use of interrupted sutures tension on the tissues was eliminated. (4) No retention sutures were used. Wound disruptions have been reduced to less than 1 per cent and postoperative hernias have decreased and are, also, in the neighborhood of 1 per cent."

Discussed by **Samuel C. Harvey,** New Haven, Conn.; **A. O. Singleton,** Galveston, Tex.; **Roscoe R. Graham,** Toronto, Ontario; **Walter D. Wise,** Baltimore, Md.; **Charles C. Lund,** Boston, Mass.; and **P. E. Truesdale,** Fall River, Mass. The discussion related to various phases of wound disruption, including suture material, knots, surgical technique, infection, hemorrhage, and the importance of the selection of anatomic incisions, as well as allergy, low vitality, etc.

Observations on the Mode of Action of Sulfanilamide and Its Application to Surgical Infections: John S. Lockwood, New York, N. Y.—"Clinical and experimental observations from a wide variety of sources have demonstrated the spectacular therapeutic effectiveness of sulfanilamide in certain types of lesion, and lesser degrees of effectiveness in other types. The explanation of such variations, the rational application of sulfanilamide to specific clinical lesions, and the interpretation of therapeutic results await the formulation of a precise understanding of the mode of action of the drug. Laboratory and clinical evidence will be presented to support the belief that sulfanilamide destroys the invasiveness of organisms having or potentially having this property. Sulfanilamide acts directly or indirectly on invasive organisms to prevent their utilization of tissue and serum protein as a source of nitrogen for reproduction, which is a capacity essential to organisms in producing invasive lesions. It does not bring about bacterial death if peptones, or similar substances found in devitalized tissue, are present to satisfy the nutritional requirements of nitrogen metabolism. Sulfanilamide in high dilution will bring about rapid death of virulent hemolytic streptococci inoculated into peptone-free serum, but the addition of small amounts of peptone prevents such action. By inference from these experiments and from clinical experience, it is possible to conclude that sulfanilamide will act with maximal effectiveness in lesions characterized by minimal traumatic or bacterial necrosis of tissue, and least effectively in lesions well supplied with products of tissue breakdown."

The Chemotherapy of Bacterial Infections: Perrin H. Long and **Eleanor A. Bliss,** Baltimore, Md.—"During the last two years several hundred patients suffering from streptococcal, meningococcal, gonococcal, and certain other bacterial infections have been treated in the wards of the Johns Hopkins Hospital with sulfanilamide or 'prontosil solution.' In general, the therapeutic effects of sulfanilamide in the treatment of susceptible infections have been brilliant. Certain of the treated patients have shown various toxic manifestations of the drug, such

as nausea, vomiting, cyanosis, acidosis, skin rashes, fever, acute hemolytic anemia and agranulocytosis. It will be our purpose in this communication to discuss methods of administration of sulfanilamide or 'prontosil solution,' the indications for the use of these drugs, the toxic effects noted as the result of sulfanilamide therapy, and the therapeutic effects obtained in certain bacterial diseases.'' Discussion by **Dean Lewis**, Baltimore, Md.

The Action of Sulfanilamide Upon Hemolytic Streptococci: Dr. Champ Lyons, Baltimore, Md., and **Richard H. Miller**, Boston, Mass.—''Experiments are reported to demonstrate that sulfanilamide acts upon hemolytic streptococci to: (1) Prolong the 'lag phase' of growth without being truly bacteriostatic or bactericidal; (2) alter the physicochemical structure of the capsule; (3) attenuate the virulence of the organisms. Clinical and laboratory results are correlated to demonstrate: (1) Patients with no antibacterial antibody and highly virulent organisms require large doses of sulfanilamide over a long period of time (7 to 10 days). (2) Patients with no antibacterial antibody and less virulent organisms require large doses of sulfanilamide over short periods of time (48 to 72 hours.) (3) Patients with antibacterial antibody require lower doses over short periods of time (48 to 72 hours), regardless of the virulence of the organism.''

These papers were discussed freely with many favorable reports of its use and very few unfavorable reports in the treatment of most all varieties of infection. There seem to be, as yet, few rules restricting its use.

Regional Ileitis: Claude F. Dixon, Rochester, Minn.—''Regional ileitis may involve either the small or large intestine. Cause unknown. Terminal ileum is most common site. The disease is being discovered much more often than in the past and is becoming known as a distinct entity. The complications are perforation into other organs and fistula formation. The treatment is surgical.'' He reports 30 cases, 87 per cent in the ileum, ages 30 to 40. Many have fistulas. With 39 cases of Pemberton and Brown there were 69 cases. Of these 25 had ileo-colostomy and 5 were cured; 40 cases were resected, 4 died, 34 are well. Advocates one or two stage operation. He prefers to call the disease Regional Enteritis.

Discussed by **Horace Binney**, Boston, Mass.; **E. P. Lehman**, University, Va.; **H. H. Kerr**, Washington, D. C.; **C. G. Mixter**, and **John Homans**, Boston, Mass.—Some cases were reported cured by no treatment, while others were more radical. Also, even after resections, some cases of recurrence were reported. The etiology was unknown.

The Rapid Control of Intracranial Pressure: Erwin R. Schmidt, Madison, Wis.—''Our present methods to control increased intracranial pressure require some time to be effective and depend on physiologic principles. The method we wish to present depends on mechanics alone, is rapid, and is effective in a large percentage of the cases. By means of a ventricular puncture, a drain is inserted and the cerebrospinal fluid can be removed and any fluid that is produced can escape, making the reduction permanent as long as the drain remains in place. We have used it in twenty cases for the following indications: (1) preoperative reduction of cranial pressure to help stabilize the patient and to prevent sudden changes at the time of operation; (2) postoperatively to prevent pressure developing and making for a smoother convalescence; (3) where operation has failed to remove the cause of the pressure, to make a smoother convalescence and to put the patient in better shape for radiation therapy; (4) to aid in preoperative diagnosis; (5) by using a ventricular drain, emergency operations following ventriculography are not necessary; (6) cerebral hernia can be controlled by ventricular drainage.'' Ureteral

catheter used and may be changed occasionally. There is slight danger of infection. There are twenty-four cases reported in which it was used.

A. W. Adson, Rochester, Minn., discussed the paper and also recommended the drain.

The Treatment of Cranial Osteomyelitis and Brain Abscess: A. W. Adson, Rochester, Minn.—"Osteomyelitis of the cranial bones develops from extending infections of the nasal sinuses, mastoids, contaminated compound fractures of the skull and infections of the scalp. Denuded skull areas resulting from lacerated scalp wounds, electric burns and the removal of the scalp with a tumor invariably become osteomyelitic and require similar treatment to that employed in a frank osteomyelitis of cranial bones. The infection may involve either one or both tables of the skull. It usually spreads in a serpiginous course along the diploic canals, but it can communicate superficially with the periosteum and scalp and internally with veins of the dura and brain through the emissary venous system. Prompt adequate drainage and sequestrectomy are necessary to control the infection and to prevent cerebral abscess formation. However, if a brain abscess has developed with the osteomyelitis, the disease should be treated as two distinct lesions. The osteomyelitis deserves prompt surgical attention; whereas, the brain abscess should be treated as a progressing furuncle or abscess in other parts of the body. The treatment consists of supportive measures until the walling-off process has taken place. The time required for encapsulation depends upon the virulence of the organism and the ability of the patient to develop an immunity. This period varies from ten days to three weeks. The initial symptoms of a high septic temperature, leucocytosis, general malaise, and stupor begin to subside as soon as immunity develops. The patient appears to improve but fails to make a complete recovery. The daily temperature rises slightly above normal. The leucocytosis averages about 12,000 and the cerebral symptoms improve except those due to increased intracranial pressure and cerebral localization. The most suitable time to drain an abscess is when immunity and encapsulation have been accomplished since there is less danger of spreading the infection and a greater opportunity to relieve the increased intracranial pressure."

Discussed by **T. C. Grant,** Philadelphia, Pa., who prefers the smaller openings and repeated tapping of the abscess or small drain. **Gilbert Horrax,** Boston, Mass., uses both methods and sometimes extirpates the abscess. **J. M. Mason,** Birmingham, Ala., reported a case of osteomyelitis from an electric burn and advocates early removal of devitalized outer table of skull.

The Alteration of Tetanus Toxin Within the Spinal Cord: Warfield M. Firor and **Austin Lamont,** Baltimore, Md.—"A technique has been devised for the accurate injection of minute amounts of tetanus toxin into various parts of the dog's spinal cord. By this procedure it is possible to produce pure reflex motor tetanus without the slightest evidence of peripheral spasm or muscular rigidity. Furthermore, the intraspinal injection of a fraction (1/120 to 1/100) of an ordinary lethal dose is always followed by the death of the animal. The mechanism of death is respiratory failure. The obvious explanation that the toxin passes up the cord is not tenable because death occurs when the toxin is introduced into the distal segment of a transected cord. In four instances it has been possible to cause the death of other dogs by intramuscular injections of the segment of cord in which a sublethal amount of tetanus toxin had been previously deposited. The intracerebral injection of minute amounts of tetanus toxin has not as yet produced symptoms or caused death. The intravenous administration of a hundred times the neutralizing dose of antitoxin one hour after an intraspinal injection fails to halt

the progress of symptoms or to prevent death. Adequate controls have been carried out for each experiment. It seems that tetanus toxin is altered in the spinal cord of dogs and that a more potent substance is formed which causes death by respiratory failure.''

Discussed by **Peter Heinbecker,** St. Louis, Mo., who was unable to say that local tetanus was not in muscles but toxin was in the central nervous system definitely; also, that tetanus toxin is easily changed by dilution with peptones, etc. Experimentally, if taken from crushed cord and modified, it may become more virulent. Tetanus toxin acts as strychnine on the central nervous system.

Sensory Denervation of the Bladder for Relief of Intractable Vesical Pain: W. J. Merle Scott, Rochester, N. Y., and **Carlisle F. Schroeder,** Detroit, Mich.—''The scant and rather conflicting literature concerning the relief of intractable bladder pain is reviewed. The previous methods of accomplishing this have not been very satisfactory. This paper reports ten cases of tuberculosis of the bladder and interstitial cystitis, in which a satisfactory sensory denervation of the bladder has been achieved. A standardized operation is offered to relieve this excruciating pain.'' In the three interstitial cystitis cases there was no relief after sympathectomy because in those the fundus of the bladder, rather than the trigone, was involved. The denervation consists of removal of the suprahypogastric sympathetic plexus, also denervation of the hemorrhoidal artery. The denervation may be reinforced by small amounts of alcohol in the spinal canal. Discussed by: **Loyal Davis,** Chicago, Ill. He approved the procedure but felt it would not succeed 100 per cent.

Injuries to the Recurrent Laryngeal Nerve in Thyroid Operations: Their Management and Avoidance: Frank H. Lahey and **W. B. Hoover,** Boston, Mass.—''Variations in the recurrent nerve in normal states, variations in pathological states, variations in developmental defects. Relation of loss of voice and breathing difficulties to nerve injuries. Anatomical points at which nerves most often injured and reasons why. Method by which injury to nerves may be avoided. Results of complete dissection of the recurrent laryngeal nerve in all thyroid operations for three years. Number of injuries reduced from 3 per cent to ½ per cent. Report of case in which both recurrent laryngeal nerves severed ten months previously were resutured. Cannot always depend upon sutures. Description of an operative procedure devised by Dr. Walter B. Hoover, successfully applied in six cases for bilateral abductor paralysis together with reports of end results, tracheotomy tubes dispensed with postoperatively in all cases. It consists of submucous excision of scar of cord by laryngofissure. Possibility of anastomosing nerves other than recurrent nerves in recurrent laryngeal paralysis with gaps too large for direct anastomosis, as the phrenic.''

Dr. Hoover: Paralysis of one cord causes loss of voice for a while but recovers in few months while loss of both cords results in great narrowing and can hardly do without tracheotomy by laryngofissure and dissecting out the cord gives room and relief.

Discussed by **Frederick A. Coller,** Ann Arbor, Mich.—More recurrent laryngeal nerves are injured than we think, maybe unrecognized. Coller also advises exposure of the nerve in thyroidectomy. The right nerve is more often injured and should be exposed. Also discussed by **Mont R. Reid,** Cincinnati, Ohio; **Edward D. Churchill** and **Elliot C. Cutler,** Boston, Mass.

Progressive Exophthalmos Associated with Disorders of the Thyroid: Howard C. Naffziger, San Francisco, Calif.—''In 1930, a patient with severe and rapidly

progressive exophthalmos, which began some time after a thyroidectomy, presented herself with failing vision, some swelling of the optic disks, and threatened desiccation of the cornea. Investigation of the literature indicated no known pathologic cause for the condition, but a wide variety of treatments, varying from sympathectomy to sutures of the lids, had been employed in attempts to palliate the condition. For our patient we planned a direct investigation of the orbit which would also be a decompressive operation. A myopathy was found to be responsible for the proptosis, and the characteristic pathological picture was revealed on the examination of small biopsy specimen. The treatment was highly satisfactory and a similar operation was later performed on the opposite side in this same patient. Since the presentation of this first case, a number of other patients have been operated on, and a large number of examinations have revealed the constancy of the pathological change in the muscles. The original operation has been modified to increase its effectiveness, and attempts have been made by experimental study, to throw light on the etiology of the condition. To date these studies have not been conclusive, but, in connection with the clinical relationships involved in progressive exophthalmos, they have thrown interesting sidelights on the condition.''

Discussed by **Thomas M. Joyce**, Portland, Ore.; **Martin B. Tinker**, Ithaca, N. Y.; **Harry B. Zimmerman**, St. Paul, Minn., who all praised the operation. **Frank H. Lahey**, Boston, Mass., reported superior cervical sympathetic ganglionectomy in mild cases of exophthalmos to be a good procedure.

Amount of Thyroid Remnant in Operations for Diffuse Toxic Goiter: Morris K. Smith, New York, N. Y.—''Amount of normal gland that will protect against permanent hypothyroidism is very small. Development of modern radical resection. Review of opinions of various surgeons which varied. A study of the relation of the size of remnants left at operation in a series of cases (about 70) to the postoperative course. As far as carried out, it indicates that in general among those left with smaller remnants there was a lower incidence of postoperative hyperthyroidism. However, if the series is divided into two groups according to the size of the remnant the combined postoperative metabolic curve of the group with larger remnants is as satisfactory as that of those with lesser remnants. Four to 10 gm. of thyroid tissue depending on the size of gland, severity of intoxication and response to iodine should ordinarily meet the indications.'' The gland regenerates greatly. There is some danger of taking too much, producing hypothyroidism. We leave more than we think usually, 4 to 6 gm. enough to leave.

Discussed by **W. B. Parsons**, New York, N. Y., and **M. B. Tinker**, Ithaca, N. Y. Both urged conservative operation and second operation rather than myxedema.

Further Observations Upon Arteriovenous Aneurysms and Abnormal Arteriovenous Communications: Mont R. Reid and **Johnson McGuire**, Cincinnati, Ohio.—''Since publication of our series of arteriovenous and cirsoid aneurysms in 1926, 30 additional cases have been studied. Interesting observations have been made upon the effect of such lesions on the heart, circulation time, blood volume, venous pressure, etc. Conditions have arisen which made it impossible to use any of the standard procedures for operating upon arteriovenous aneurysms. Two additional operative procedures have been devised where the fistula cannot be directly attacked. One of these is the twisting of the vein to occlude the fistula, and the other is direct transfixation closure of the fistula by passing a double suture directly through the vein and tying it in a V-shape so as to obliterate the opening. Acute and chronic experiments have been undertaken in the laboratory. In the acute experiments artificial anastomosis between the aorta and the vena cava have been made and the

effects noted. A Venturi tube, so constructed as to measure the volume of blood flow, was placed in the vena cava between the fistula and the heart in two instances. A tremendous increase in the volume of blood being returned to the heart through the vena cava was recorded. We are not able to demonstrate, either experimentally or clinically, a marked rise in venous pressure between the fistula and the heart, as has been reported by some other investigators. Neither are we convinced that the immediate effect upon the heart is a decrease in its size. In addition to the acute experiments we wish to report some observations made upon chronic cases of arteriovenous fistula produced in dogs.'' Detailed report of cases with drawings of the technique of each operation was shown.

Discussed by **James M. Mason,** Birmingham, Ala., who recited history of the discovery of the relations of arteriovenous fistula and heart disease. He also reported cases of his own. **Edwin P. Lehman,** University, Va., reported an interesting case of the abdominal aorta and vena cava in which both were ligated but death soon followed.

The Use of Heparin in Thrombosis: W. E. Gallie, D. W. G. Murray, and **Charles H. Best,** Toronto, Ont.—''Heparin was discovered in 1916 and proved to be an anticoagulant. Attempts at using it on human beings showed that it was toxic and unsuitable for clinical use. It has now been purified and is obtained in crystalline form with a potency of about 500 units per mg. Experiments were started in 1932, to determine: (1) Toxicity; with the impure form of heparin, toxic symptoms were produced in animals, but as the heparin became purified the toxic symptoms soon disappeared; with the crystalline form in more than 230 clinical cases there have been no toxic effects. (2) The effect of heparin on thrombosis: (a) Experiments were undertaken in which veins were injured by (*1*) mechanical and (*2*) chemical means; the efficacy of heparin was studied. (b) In 230 clinical cases where the needle was lying in the lumen of the vein for periods from three days to three weeks, thrombosis did not occur. (c) With end-to-end suture of arterial and venous grafts in arteries, 60 per cent became occluded. Where heparin was given all remained patent as long as injections continued and many for months afterwards. (d) When an embolus was placed in an artery and left for forty-eight hours and then removed, all vessels remained patent, where heparin was given intravenously. (e) In transplantations of the kidney into the neck the circulation was maintained more frequently when the intravenous injection of heparin was employed. Application: heparin has been administered postoperatively to cases where thrombosis in veins and resulting pulmonary embolism was in danger. In 230 cases in which it has been given, there has been no evidence of thrombosis or embolism. In cases of thrombophlebitis, the symptoms were rapidly improved after administration. It is suggested that heparin might be useful in other diseases where thrombosis is a factor.''

Heparin is not toxic. It prevents thrombosis and decreases clotting time, but clotting time returns to normal quickly after drug is stopped. Experiments where sections of vein grafted into defect in artery will not clot with heparin and graft lives. Also possibly great good may result after embolectomy to prevent reclotting if heparin is given for two weeks. Also, it is given postoperatively to prevent pulmonary embolism. Thrombophlebitis (28 cases) improved more rapidly with heparin. There are possibilities of great good in coronary thrombosis, sinus thrombosis, etc.

Discussions: Dr. Best said the purification of heparin made it possible for clinical use. **H. Lilienthal,** New York, N. Y., recommended leaches to prevent thrombosis, and has had good results in thrombophlebitis. **F. W. Bancroft,** New

York, N. Y., referred to his work with sodium diosulfate in the prevention of postoperative thrombosis. He also thought that high blood proteid and fat content was a factor in thrombosis. **Mont R. Reid,** Cincinnati, Ohio, discussed the use of heparin in experimental surgery.

Spontaneous Rupture of the Epigastric and Internal Mammary Arteries Within the Rectus Muscle: Robert L. Payne, Memphis, Tenn.—"Interest in this condition centers around the apparent rareness of the lesion, together with the comparative difficulty in diagnosis. Rupture of the internal mammary or epigastric artery within the rectus muscle or sheath may be due to direct or indirect forces which are clear cut as a contributing factor. However, many lesions appear spontaneously, though there is some doubt but what indirect trauma may be a factor in every instance. The clinical syndrome is quite typical, but because of its rarity is commonly treated under a doubtful or mistaken diagnosis, and often neglected over a sufficient period of time to permit extensive extravasation into the muscle with accompanying pressure necrosis, infection, and abscess formation due to neglect." It should be recognized and often operation done early. Discussed by **Mont R. Reid,** Cincinnati, Ohio, who endorsed the author's views.

A Study of the Lymphatics in Carcinoma of the Rectum: Vernon C. David and **R. K. Gilchrist,** Chicago, Ill.—"As a result of this study two conclusions have been drawn: (1) That the number of glands involved with carcinoma cannot be determined except by careful preparation and dissection of the specimen. In connection with this we will describe briefly a new technique for the same. (2) The average number of glands examined in specimens of carcinoma of the rectum run between 10 and 25, as reported in the literature. By the methods described we have been isolating between 50 and 60 glands and have found an average involvement in the resected specimens of about 70 per cent as compared with 35 to 45 per cent described usually. Some rather interesting facts about the method of spread have developed from this study. Naturally, this whole subject brings up the question of prognosis based on involvement of glands by carcinoma at the time of operation. If prior statistics have been based on an average involvement of 35 to 45 per cent of glands, then a new viewpoint of the whole subject of prognosis on a basis of gland involvement will have to be taken." Small tumors may show many infected glands, and vice versa. Squamous cell and growth may spread to pelvic glands.

Dr. David emphasized the important points of the paper. **Harvey B. Stone,** Baltimore, said presentation shows clearly that extensive resection is necessary to get all infected glands as some are often very high.

The paper was also discussed by **R. Colp,** New York, N. Y., and **E. W. Archibald,** Montreal, Que.

The Treatment of Intraperitoneal Abscess Arising from Appendicitis: Edwin P. Lehman, University, Va., and **William H. Parker.**—"A study based upon 1,069 cases of acute appendicitis admitted from 1933 to 1937 inclusive. Great care has been directed towards definition of three groups of appendicitis: (1) simple, (2) with abscess, (3) with diffuse peritonitis. No cases are included in the last two groups without actual established peritonitis, whether or not perforation had occurred. The study is directed towards the treatment of Group 2, comprising 181 cases. The factors studied are: (1) mortality, (2) complications, (3) hospital days, (4) fever days, (5) drainage days. Positive conclusions are stated on only those differences in data which can be shown by statistical methods to be significant. The abscess cases are divided into five groups according to the therapeutic proce-

dures carried out. Conservative treatment of appendiceal abscess without operation at any time during the acute phase gives by far the best results if it can be carried out successfully. However, the total result of the method must be judged on a combined group, including both the successfully completed cases under conservative treatment and those in which operation is later forced by unfavorable progress of the disease. Comparison between this combined group and the group in which operation was done as an elective procedure leads to the conclusion that the initiation of conservative treatment in appendiceal abscess is the method of choice.''

Discussed by **F. A. Coller,** Ann Arbor, Mich., who agreed with the conservative treatment advocated. **Shelton Horsley,** Richmond, Va., preferred prompt operative treatment generally and showed statistics justifying the plan. **T. G. Orr,** Kansas City, Mo., and **Roscoe R. Graham,** Toronto, Ont., also waited and treated abscesses without operation. **O. H. Wangensteen,** Minneapolis, Minn., agreed but warned against prolonged delay when the abscess was large and the patient continued febrile. **A. O. Whipple,** New York, N. Y., thought that there was danger in leaving the impression that delay or nonoperative treatment was advisable as a general rule because it might lead to late rather than early operation in appendicitis.

Epidermoid Cysts of the Spleen: Albert H. Montgomery, Eugene T. McEnery, and **Albert A. Frank,** Chicago, Ill.—''Epidermoid cysts of the spleen are usually large, solitary, and lined with stratified pavement epithelium with prominent intercellular bridges. No other epidermal or dermal elements are found. They have been reported as weighing as much as 3 kg. and to have contained 1,500 c.c. of watery chocolate fluid usually containing cholesterol. The general structure is strikingly similar from trabeculated inner surface, to fibrous capsule and secondarily compressed spleen. The splenic tissue is usually unaltered except for gross compression and fibrous replacement adjacent to the cyst capsule. All clinical symptoms may be explained on the basis of compression alone. Epidermoid cysts of the spleen have been considered relatively rare anatomic entities, and few cases have been reported in the literature. No satisfactory explanation of their origin has been offered. With the assumption that epidermoid epithelium is necessarily ectodermal in origin, the necessity arises of accounting for ectoderm in an organ presumably arising from mesenchyme. Various theories of the origin of epidermoid cysts of the spleen will be discussed. Two cases are reported with clinical and pathological findings. The lesion seems to be so rare it is thought worth while to report these two additional cases and perhaps stimulate the report of others by members of the association.''

Mediastinitis Following Cervical Suppuration: Herman E. Pearse, Jr., Rochester, N. Y.—''Infection of the neck that invades the cervical spaces may gravitate into the chest and cause a mediastinitis. The pathways of this spread have been studied and an operation to prevent it has been suggested. When suppuration in the mediastinum develops, it may be drained through the neck, which results in recovery of about two-thirds of the patients treated. The management of this type of suppurative mediastinitis is discussed from experience with anatomical dissection and the treatment of clinical cases both personal and those derived from the literature.'' A study of 110 cases in the literature and 11 cases of Pearse's own were reported; 71 in the retrovisceral space and 21 in the carotid sheath and 8 pretracheal. Drain in the neck in front lateral to esophagus. A 35 per cent mortality.

Discussions: **E. D. Churchill,** Boston, Mass.: Perforation of esophagus by endoscopy which is fatal unless immediately drained. The posterior approach may

be necessary if infection low in mediastinum. **M. B. Tinker,** Ithaca, N. Y., and **Howard Lilienthal,** New York, N. Y., urged early operation. **John Alexander,** Ann Arbor, Mich., discussed the value of the anterior incision in the early cases and the posterior approach in cases deep in the mediastinum. **O. H. Wangensteen,** Minneapolis, Minn., suggested the value of x-ray showing air in mediastinum soon after perforation. He also advised posture in drainage.

The Iodine Metabolism in Exophthalmic Goiter: George M. Curtis, Columbus, Ohio.—"The development of suitable micromethods has permitted analysis of the iodine content of the blood, urine, feces, and sweat, as well as the content of the thyroid gland. As a consequence we have investigated the total iodine metabolism of patients with exophthalmic goiter. The blood iodine is greatly increased over normal. The urinary excretion of iodine is increased. There is also an increased loss of iodine, particularly in the feces, and in the sweat. If the intake of iodine in the food, water, and air is accurately determined, it is found that patients with exophthalmic goiter are in a definite increased negative iodine balance. Iodine depletion thus occurs in the usual progress of this decrease." Discussed by **Frank H. Lahey,** Boston, Mass., who said some patients have low blood iodine with high metabolic rate, which is contrary to the usual.

REVIEW OF THE THIRTY-EIGHTH ANNUAL MEETING OF THE AMERICAN ASSOCIATION OF PATHOLOGISTS AND BACTERIOLOGISTS, ATLANTIC CITY, N. J., MAY 3 AND 4, 1938

E. T. Bell, M.D., Minneapolis, Minn.

(From the Department of Pathology, University of Minnesota Medical School)

DALE REX COMAN (by invitation), **Morton McCutcheon,** and (by invitation) **Paul T. DeCamp,** Philadelphia, Pa.: **Chemotropism Induced by Streptococcus Hemolyticus in Leucocytes From Normal and Immune Animals.**—Chemotropism was studied on the warm stage. The polymorphonuclear leucocytes moved toward the bacteria at an average speed of 10 to 15 microns per minute. There was no significant difference between the behavior of the leucocytes from immune and nonimmune animals. Antibodies in the serum therefore play no role in chemotropism.

Max M. Strumia, Bryn Mawr, Pa.: **Serologic Studies in Children Before and After Vaccination With the Scarlet Fever Streptococcus Toxin.**—Strumia studied the serologic reactions in children before and after vaccination with scarlet fever streptococcus toxin. He found no significant serologic differences between the Dick negative and the Dick positive stages.

Jerome T. Syverton and **George Packer Berry** (by invitation), Rochester, N. Y.: **Multiple Virus Infection of Individual Host Cells.**—Syverton showed that a single cell could harbor more than one virus. This judgment was based upon the occurrence of inclusion bodies within the cells. A cell may harbor the herpes virus (intranuclear inclusion) and the vaccine virus (cytoplasmic inclusion). He also used

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the B virus and the myxoma virus. A single cell in some instances harbored three viruses. Tumor cells are readily parasitized by viruses.

Robert J. Parsons and **John G. Kidd** (by invitation), New York, N. Y.: **Oral Papillomatosis of Domestic Rabbits: A Virus-Induced Disease.**—The authors found a spontaneous papilloma on the under surface of the tongue of domestic rabbits. This occurs in the form of multiple papillomas of benign structure. In 700 domestic rabbits, 16.2 per cent had this form of papilloma. When the skin of the rabbit is tarred, the incidence of spontaneous papilloma on the under surface of the tongue increases to 48 per cent. They found that the papillomas may be transmitted by tattooing the filtrate of the tumors on the under surface of the tongue of the rabbit. Papillomas do not grow in other situations. The growth is different from the Shope papilloma, which does not grow on the under surface of the tongue. Immunologically, this papilloma is also separable from the Shope papilloma.

O. C. Woolpert, F. W. Gallagher, Leona Davis (by invitation), and **N. Paul Hudson: Propagation of the Virus of Human Influenza in the Guinea Pig Fetus.**—It was shown that the guinea pig fetus may be used for the growth of the human strain of the influenza virus. The fetus was inoculated intracranially. The fetal lung may be used for inoculation since it contains the virus.

A. Packchanian (by invitation), Washington, D. C.: **The Prevalence of Infectious Jaundice in the United States as Determined by the Agglutination and Animal Inoculation Tests.**—The author stated that Weil's disease is rather widely distributed in the United States, although he does not think that all cases of infectious jaundice are due to leptospirae. He based this statement upon agglutination tests and animal inoculations. He found that field mice are highly susceptible to the spirochetal infection. He studied several epidemics of infectious jaundice, but he did not make it clear what percentage of cases of epidemic jaundice are Weil's disease.

Dudley A. Irwin, Toronto, Ontario: **The Experimental Prevention of Silicosis by Metallic Aluminum.**—Irwin showed experimentally that the addition of 1 per cent of alum to silica prevents the development of silicosis in animals. The alum apparently prevents silica from going into solution. He indicated that some attempts were being made to mix alum in silica dust for the protection of workmen.

Earl B. McKinley, Washington, D. C.: **The Tuberculin Reaction and Its Significance in Leprosy.**—McKinley believes that the high incidence of positive tuberculin reactions in lepers is due to associated tuberculosis and not to the leprosy itself.

Edgar H. Norris, Minneapolis, Minn.: **The Cytology of the Human Parathyroid Glands.**—Norris demonstrated the various types of cells that occur in the normal parathyroid glands and in parathyroid adenomas. He believes that increased vacuolization of the cytoplasm indicates functional activity.

Robert A. Moore and (by invitation) **Allister McLellan,** New York, N. Y.: **A Histologic Study of the Effect of the Sex Hormones on the Human Prostate.**—A few patients with hypertrophy of the prostate were treated with testosterone and others were treated with estrin. Neither of these hormones produced any definite effect upon the enlarged prostate.

Paul R. Cannon and (by invitation) **E. M. K. Geiling,** Chicago, Ill.: **Pathologic Effects of Elixir of Sulfanilamide Poisoning.**—Cannon reported results of postmortem examination in a child 3½ years of age who had died from the administration of elixir of sulfanilamide. He also reported the findings in a man 64 years of age who died from similar poisoning. The most striking change was an extreme hydropic degeneration of the cells of the convoluted tubules of the kidneys and of the hepatic cells.

Harry S. N. Greene and (by invitation) **John A. Saxton, Jr.,** Princeton, N. J.: **Uterine Adenomas in the Rabbit.**—Greene studied spontaneous adenocarcinomas of the uterus in rabbits. He observed a number of these spontaneous tumors. The animals finally die of metastases. The gross appearances, as well as the microscopic structure, are closely similar to the corresponding tumor in women. He was unsuccessful with primary transplantation experiments except when the tumor was inoculated into the eye. In this situation it grew well and after several such transplants it grew readily in other parts of the body. It was often successfully transplanted to guinea pigs and rats by intraocular inoculation.

Peyton Rous and (by invitation) **John G. Kidd,** New York, N. Y.: **A Comparison of the Virus-Induced Rabbit Tumors With the Tumors of Unknown Cause Elicited by Tarring.**—Rous studied tar papillomas of the rabbit's ear as well as Shope papillomas. When Shope papilloma virus is infiltrated into the ear, tarring causes enormous growth of papillomas. He believes that all carcinogenic agents prepare the soil for the virus which causes the tumor. He believes that the tarring of the skin prepares the way for the invasion into the cells of the virus of unknown origin.

William H. Feldman and (by invitation) **A. H. Baggenstoss,** Rochester, Minn.: **The Residual Infectivity of the Primary Complex of Tuberculosis.**—The authors studied old healed primary tuberculous lesions microscopically and by animal inoculation. They found that nearly all of these healed lesions failed to produce tuberculosis in guinea pigs, even though many of them had well-formed tubercles about the periphery of the old scar. They were inclined to believe that these small tubercles about the scar were due to silicosis.

Benjamin J. Clawson, Minneapolis, Minn.: **The Effect of the Primary Pulmonary Focus Upon the Progress of Experimental Pulmonary Tuberculosis.**—Clawson demonstrated that by direct inoculation of B.C.G. into the lungs of rabbits a lesion is produced which resembles the lesion in primary pulmonary tuberculosis except that there is no involvement of the regional lymph nodes. Animals with this pulmonary lesion show a striking resistance to virulent tubercle bacilli.

William E. Ehrich, Philadelphia, Pa.: **The Renal Lesion in Cytotoxic Glomerular Nephritis (in Rabbits).**—Ehrich immunized rabbits with kidney extracts and then injected them intravenously with the corresponding antigen. He produced acute glomerulonephritis and in some instances the lesions progressed to a stage at which it might appropriately be called chronic glomerulonephritis.

REVIEW OF THE THIRTY-FIRST ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, ATLANTIC CITY, N. J., MAY 2, 1938

E. T. Bell, M.D., Minneapolis, Minn.

(From the Department of Pathology, University of Minnesota Medical School)

E **M. BURKE**, Buffalo, N. Y.: **Sarcoma of Soft Tissues.**—Burke reported on 201 cases of sarcoma of the soft tissues. There were 107 males and 94 females; 30 per cent of the patients were under 30 years of age. The lower extremities were involved most frequently. The 5-year survivals were as follows: grade 1 sarcoma, 73.2 per cent; grade 2, 42 per cent; grade 3, 14 per cent.

Leonell C. Strong, New Haven, Conn.: **VII. The Liquefaction of Spontaneous Tumors of the Mammary Gland in Mice by Heptyl Aldehyde.**—Strong studied the influence of heptyl aldehyde upon spontaneous tumors of the mammary gland in mice. The drug was given in the diet, about 1 drop to 2 gm. of food. The dosage was adjusted to the weight loss. It was given periodically over a long period. The drug produced liquefaction of the tumors, often with collapse and shrinkage of the tumor mass. The average survival time of the treated animals was 83 days, while that of the controls was 55 days. The tumor finally becomes resistant to the chemical agent and no longer responds. Two treated animals were still alive at 160 days. Microscopically he noted a lymphocytic and polyblastic invasion of the disintegrated tumor. The periphery of the tumor, as well as its central portion, showed the effects of the chemical agent.

S. H. Gray and **G. Gruenfeld** (by invitation), St. Louis, Mo.: **The Production of Carcinoma and Sarcoma by the Subcutaneous Injection of Benzpyrene.**—Both carcinomas and sarcomas were produced by benzpyrene. The chemical agent was given in 4 per cent solution in lard or as a dry powder in capsule. Tumors were obtained with the dry powder as well as with the lard. They introduced 15 mg. of dry powder subcutaneously. Usually there was ulceration of the skin. Both carcinoma and sarcoma were produced and sometimes both types of malignancy were present in the same growth. The ulcer was at first benign but later became malignant. There were no metastases.

A. G. Ide (by invitation), **R. A. Harvey** (by invitation), **F. W. Bishop** (by invitation), and **S. L. Warren**, Rochester, N. Y.: **A Study of the Capillary Development Around the Tumor Transplant in a Window in the Rabbit's Ear; a Demonstration of One of the Common Methods of Metastasis.**—The investigators transplanted a sarcoma into the subcutaneous tissues of the ear of a rabbit and studied the changes through a transparent window which covered the wound. They presented an excellent motion picture showing the growth of the transplanted tumor and the manner in which metastases are formed. The large capillaries which grew into the tumor showed oscillation of the blood current to-and-fro, and these movements detached some of the tumor cells and carried them into the circulation.

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Madge Thurlow Macklin (by invitation), London, Ontario: **Can a Study of Human Cancer Teach Us Anything of Value Concerning Its Inheritance?**—Macklin believes that a great deal can be learned about the hereditary transmission of tumors from human material. She stressed the important influence of age in each type of neoplasm and pointed out that each tumor has its own preferred age incidence. She cited the well-known hereditary transmission of retinoblastomas and the carcinomas in xeroderma pigmentosum. Her data also indicated a strong hereditary influence in carcinoma of the breast. She indicated that each tumor must be studied separately.

G. E. Hall (by invitation) and **W. R. Franks**, Toronto, Ontario: **Acetylcholine and Endogenous Carcinogenesis.**—Tumors were produced by acetylcholine, a substance which is formed normally within the body. They obtained one sarcoma of the femur in a dog and sarcomas were obtained readily in rats. The chemical substance was introduced subcutaneously. The first tumor appeared at the fifth month. This work is of interest in that acetylcholine is of physiologic origin, as is estrin.

J. T. Syverton, R. A. Harvey (by invitation), **G. P. Berry**, and **S. L. Warren**, Rochester, N. Y.: **The Inactivation of Papilloma Virus (Shope) by Roentgen Radiation With Some Correlated Observations on Other Viruses and Bacteria.**—The Shope papilloma of the ear of a rabbit is easily destroyed with 3,500 r. The effect is the same whether the radiation is given all in one dose or fractionally. When a suspension of the virus is irradiated, an enormous dosage is required to kill it; 1,000,000 r. is ineffective and 14,000,000 r. is required to inactivate the virus. The investigators, therefore, concluded that radiation affected the cells and not the virus. The Shope papilloma virus is more resistant to radiation than any other virus.

Robert Hebbel (by invitation) and **E. T. Bell**, Minneapolis, Minn.: **Carcinosarcoma.**—A malignant tumor of the thyroid gland was described which formed massive metastases in the lungs. The great majority of the metastases had a structure of giant cell sarcoma, while a few had the structure of adult thyroid gland. Both of these types of tissue were present in the primary tumor. Transitions were found, which suggested that the sarcomatous tissue arose by transformation from epithelium. In the sarcomatous portions large numbers of collagenous fibers were formed by the tumor cells, indicating that, if metaplasia has occurred, it is complete. One conception of carcinosarcoma is a tumor arising from epithelial cells which undergo metaplasia in part, forming cells which have the power to produce collagenous fibers.

Halsey J. Bagg and **Flora Hagopian** (by invitation), New York, N. Y.: **The Functional Activity of the Mammary Gland in the Rat in Relation to Mammary Gland Carcinoma.**—Studies in the Wistar strain of rats showed that rapid breeding and prevention of suckling favors the production of mammary carcinoma.

J. J. Bittner, Bar Harbor, Me.: **Relation of Nursing to the Extrachromosomal Theory of Breast Cancer in Mice.**—Bittner presented further evidence indicating that the mother's milk has more influence than heredity in the development of carcinoma of the mammary gland in mice; 83.6 per cent of adult females of the high cancer strain develop carcinoma of the mammary gland, but the offspring of these high cancer females, when fostered from birth by a female of a low cancer strain, develop only 7.4 per cent of mammary carcinoma. It was shown clearly that the incidence of cancer of the breast in mice can be changed enormously without changing the genetic constitution of the animal.

Albert Claude, New York, N. Y.: **The Physical and Chemical Properties of a Chicken Tumor Agent.**—Claude purified and concentrated the active agent of the Rous sarcoma by centrifugation. The centrifugate was so concentrated that it produced tumors in a solution of 10^{-8}. The concentrated centrifugate showed about 25 per cent of lipoids. The author suggested that the virus is a lipoid protein combination.

REPORT ON THE MEETINGS OF THE AMERICAN SOCIETY FOR BIOLOGICAL CHEMISTS, BALTIMORE, MD., MARCH 30—APRIL 2, 1938

MILDRED R. ZIEGLER, PH.D., MINNEAPOLIS, MINN.

AMONG the many papers reported at this meeting, only a few have been selected which are of special interest to surgeons.

Frances L. Haven and his co-workers (University of Rochester) studied phosphorus metabolism in growing and adult white rats, with artificially radioactive phosphorus as a tracer. Data were reported giving the distribution of phosphorus fed as sodium phosphate in bones and teeth, internal organs, muscle, blood, and carcinosarcoma No. 256, as well as in the phospholipids of various organs. They found that a large portion of the phosphorus is rapidly transferred to the bony structure of the animal. The concentration of administered phosphorus rises rapidly in tumor tissue and in its phospholipid fraction, the concentration in tumor tissue a few hours after feeding being of the same order as in the phospholipid of liver and kidney and many times that of muscle.

Arthur Knudson, Stuart Sturges, and W. Ray Bryan (Albany Medical College) verified the observations of Roffo, Beard, and others that irradiation of rats with ultraviolet light over a long period of time produces malignant tumors on the ears, nose, eyes, or other exposed parts. They also carried out studies on the cholesterol content of the skin from the face, back, and abdomen of irradiated rats and determined the cholesterol content of the tumors and the blood of these animals. The total cholesterol content of the skin was increased by irradiation. The tumors from these irradiated animals were also very high in cholesterol and ran somewhat parallel with the cholesterol content of the skin from the face of the irradiated animals. However, the free cholesterol in the tumors averaged about 80 per cent, while the free cholesterol from the skin of the face of irradiated rats was 30 per cent. A few determinations on the blood of irradiated rats showed that the total cholesterol and free cholesterol content on the average was below normal.

In an attempt to elucidate the constitutional structure of the melanins, **Mona Spiegel-Adolf** (Temple University) studied the optical absorption power of various melanins for short-wave light. She used photosynthetic melanins, tumor melanins, and sepia. Ultraspectographic investigations showed distinct quantitative differences between photosynthetic melanins and the genuine melanins.

D. B. Dill, H. T. Edwards, and S. Robinson (Harvard University), in a study of metabolic adjustments, exercise, and age, observed that males from 7 to 76 years of age effectively mobilize carbohydrate to maintain the concentration of

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blood sugar near its basal value, regardless of age, in work that raises the level of oxygen consumption about seven-fold. The proportion of carbohydrate utilized in such activity was low in boys and independent of age in men. Possibly the 15-hour fast that preceded the work depleted carbohydrate reserve to a greater extent in the boys than in men, leaving the former with a less adequate supply of carbohydrate when exercise was undertaken. Five minutes after brief, severe exercise, blood sugar and lactic acid were moderately elevated in the boys and in the old men; the greatest increase occurred at the intermediate ages. The ratio of increment in blood sugar to increment in lactic acid was high in young men, low in old men.

R. N. Harger, Steven L. Johnson, and E. G. Bridwell (Indiana University) presented methods for the determination of methanol in blood, spinal fluid, urine, and body tissues.

Fred W. Oberst (United States Public Health Service) gave a simple and rapid method for the determination of morphine in the urine of drug addicts. Concentrations as low as 0.03 mg. in 25 ml. of urine are detectable. Morphine may be determined quantitatively in concentrations ranging from 0.08 to 3.0 mg. per 100 ml. of urine by their colorimetric method.

Wendell H. Griffith (St. Louis University) found that the oral or intraperitoneal administration of 50 to 150 mg. of sodium hippurate in 0.1, 0.15, or 0.31 M solution resulted in a 2 to 4° decrease in the body temperature of 50 to 60 gm. rats. The effect of hippurate was temporary and disappeared within 6 to 8 hours, while that of sodium benzoate was more marked and of longer duration. He believes these changes in body temperature to be suggestive, in view of the recent observation that both of these substances inhibited in vitro the oxygen uptake of minced tissue and of tissue slices of the rat.

Harry G. Day, Harold J. Stein, and E. V. McCollum (Johns Hopkins University) reported studies on young rats fed different levels of calcium and phosphorus which showed that calcium does not have a unique function in hematopoiesis and that excess dietary phosphorus interferes with iron utilization, probably owing to the formation of unabsorbable iron phosphate.

James M. Orten (Wayne University) presented data to show that there is a predictable normal relationship among reticulocytes, erythrocytes, and hemoglobin in rats and that definite deviations therefrom should prove as an index to abnormal hematopoiesis in the rat.

Since it has been shown that nicotinic acid and nicotinic acid amide are active in the cure of black tongue in dogs, **D. W. Woolley, F. M. Strong, and Robert J. Madden** (University of Wisconsin) investigated the anti-black tongue potency of a large series of various related compounds. Their results indicated extreme specificity of structure necessary for anti-black tongue activity. Substitution of alkyl groups in the ring on either nitrogen or carbon, or on the amide N, rendered the vitamin inactive. Their results indicate that, whereas the dog can oxidize a methyl group on the pyridine ring to a carboxyl, it cannot remove the labile alpha-carboxyl in quinolinic acid by decarboxylation nor can it hydrolyze an N-diethylamide to an acid.

Announcement

Eleventh Congress of the International Society of Surgery, Brussels, Belgium, Sept. 19-22, 1938

The Eleventh Congress of the International Society of Surgery, which, as previously announced, was to have been held in Vienna on Sept. 19 to 22, under the auspices of the German government and the cooperation of the German Surgical Society, has been abruptly cancelled by the authorities and, for reasons not yet explained, has been made impossible in Vienna. Fortunately, the transfer of the Congress from Vienna to Brussels, which was promptly effected early in July by the Executive Bureau of the International Society of Surgery, has proved of great advantage in assuring a greater success of the Congress under the liberal patronage of the Belgian Government and the enthusiastic support of the Belgian profession. *The Congress therefore will be held in Brussels without change of date, on Sept. 19 to 22, 1938.* According to the latest information received from the Secretary-General, Dr. Leopold Mayer, the scientific program will be carried out in Brussels in all its details as previously announced for Vienna. In fact, many of the reports assigned to the eminent specialists who are to open the discussions on the official questions selected for debate have been printed, and others in press will be ready for distribution in advance of the meeting.

The prospects of the elaborate Mediterranean cruise, which had been planned by the Belgian Branch of the French Navigation Company, under the direction of the International Bureau at Brussels, will be carried out in full, differing only from the itinerary originally planned for the Vienna Congress by omitting the stops at Budapest and Vienna, and substituting the return to Brussels by rail via Venice, Milan, and Basel in time to arrive in Brussels on Sept. 17 or 18. The cruise will begin in Marseilles on Sept. 4, on board the French packet, *Le Providence* (15,000 tons), and will continue along the North Mediterranean to the Black Sea, with stops at Naples, Athens, Istambul (Constantinople), Odessa (Russia), Costanze, and Bucarest (Roumania), to return to Brussels by the inland route in time for the opening of the Congress on Sept. 19.

Ample provision for sightseeing and entertainment has been assured by the appointment of active medical committees in each of the stopping places along the route, besides the assurance of success given by the long touristic experience of the Secretary-General himself, who will personally supervise the management of the cruise in its scientific and touristic aspects. During his absence, the secretarial office in Brussels will be occupied by five subsecretaries, Drs. Neumann, Appelmans, Beckers, Dejardin, and Spehl, who will attend to all the business of the Congress until Dr. Mayer's return.

It is probable that since the transfer of the Congress from Vienna to Brussels, the popularity of the Mediterranean cruise has increased, and that the demand for reservations on shipboard will be in excess of the available space. It is important, therefore, that all the Fellows of the Society, and others who may desire to join the Mediterranean cruise, should apply at once to Dr. Leopold Mayer, Secretary-General, 72 Rue de la Loi, Brussels, or directly to the Belgian office of the Compagnies Francaises de Navigation (29 Boulevard Adolph Max, Brussels).

At the present time the American Committee has given authority to the American Express Company to set up group travel direct to Brussels as well as to outline several trips which will bring the Fellows to Marseilles by Sept. 4, where, as it is described above, the French packet, *Le Providence,* will start on its Mediterranean cruise to the Black Sea.

Membership in the International Society and the Congress alone will entitle one to reduced rates and privileges over practically all the European railways and other means of transportation, on presentation of the certificate or card of membership. All the procedures required to secure reduction of fares and other privileges in the different European countries are fully detailed in the circulars recently issued to all the Fellows of the Society by the Secretary-General, the Belgian Touristic Agency of the French Navigation Companies, at 29 Boulevard Adolph Max, Brussels, and by the American Express Company.

Dr. Rudolph Matas, President.
Dr. Elliott C. Cutler, Chairman
American Committee

Book Reviews

Emergency Surgery. By Hamilton Bailey. Third Edition. Cloth. Pp. 852, with 816 illustrations, many in color. Baltimore, 1938, William Wood and Company. $14.

The author, now well-known to American students of surgery for several practical texts, has succeeded admirably in bringing together within the confines of 852 pages a comprehensive discussion of emergency surgery. The theme of the text is "when to operate, when not to operate, and how to operate under emergency conditions." In the preface to the first edition the author states: "While writing the present volume, I have pictured a patient stricken with an urgent surgical condition and a comparatively isolated surgeon called upon to carry out appropriate treatment." The scope of the present volume would lead one to believe that the author has directed the third edition in part to a more restricted audience. There are conditions, such as heart tamponade, into which it would appear eminently fitting that the "isolated surgeon" should receive as much orientation in recognizing the existence of the emergency as in how to relieve it.

The author writes in an interesting manner. The text is illustrated profusely and well and the references to literature have been chosen with care.

The author fails to point out the shortcomings of the closed method of drainage in empyema. There are too many already who believe that the application of suction to a catheter in the thorax affords perfect drainage of the free exudate without irrigation of fluid or the admission of air to the pleural pocket. The author implies that he secures continuous gastric aspiration by employment of a syringe, a method which, in this country at least, never attained any vogue. The author, too, probably will find that a water siphon is far superior for the evacuation of gas and fluid from the gastrointestinal canal. The author also endorses cecostomy as the operation of choice in acute obstructions of the colon, an operation which surgeons cannot perform in the presence of great distention and still maintain a respectable mortality. The author clings still to the idea that sudden decompression of the urinary bladder per se is hazardous. He appears to favor early ligature of the angular vein as a preventive measure in carbuncle of the face.

There is much to praise in this splendid volume and little to criticize. The experienced surgeon will find helpful suggestions in it and to the general practitioner and occasional surgeon it will be a useful guide.

The Biology of Arteriosclerosis. By M. C. Winternitz, R. M. Thomas, and P. M. LeCompte. Cloth. Pp. 142, with 116 illustrations and 59 in color. Springfield, Ill., 1938, Charles C. Thomas. $4.

This important monograph deals with the morphology of arteriosclerosis. The authors skip over quite lightly the rôle of cholesterin and its esters in the production of arteriosclerosis. It is their contention that the vasa vasorum play an all important rôle in the origins of arteriosclerosis, and that inflammatory processes and

hemorrhages in the vessel wall are the likely precursors of sclerosis of arteries. Evidence is offered by the authors which indicates that the occurrence of hemorrhage or other exudation into the interior may lead to thrombus formation upon the intimal surface with occlusion of the lumen. Mural arteries to blood vessels have been traced by the authors from three sources: (1) the adventitia, (2) the lumina of arterial branches, and (3) directly from the intimal surface of the arterial wall.

It is the expressed hope of the authors that a better understanding of the physiologic and pathologic occurrences in the arterial wall will bring arteriosclerosis out of the "limbo of degenerations into the fold of processes based on the understanding that exists for other biological phenomena."

The authors have employed histologic sections of cleared materials after intravascular injections as the basis of their study. The text is illustrated profusely and a large number of the reproductions are in natural color. This is a splendid little monograph which deserves to be studied carefully by everyone interested in the subject.

The Diary of a Surgeon in the Year 1751-1752. By John Knyveton. Edited by Ernest Gray. Cloth. Pp. 322, with 9 illustrations. New York, 1937, D. Appleton-Century Company. $2.50.

This journal kept by a young surgeon deals with his training in a London hospital and a sea voyage as surgeon's mate almost two hundred years ago. Those were stirring times and the journal is exciting in its interest. Anatomy was the basis of training for a surgeon. Operations were those of necessity and were in every sense of the word severe ordeals for all participants. The hope and despair of patients and surgeons are related with a sympathetic understanding which needs no explanation to a twentieth century audience. Generous bleeding and a free "scouring of the bowels" were the therapeutic measures directed at the feverish state attending the sequelae of operations. It seems not a little strange to us that cleanliness was so little appreciated.

Those interested in the methods of procuring anatomic material for purposes of dissection and the surgical practices of the time will find this volume exceedingly interesting and informative. Every surgeon will have much pleasure and profit in its perusal.